Volume XX Number 4

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DISEASES OF THE NERVOUS SYSTEM

A Practical Journal on Psychiatry and Neurology

APRIL
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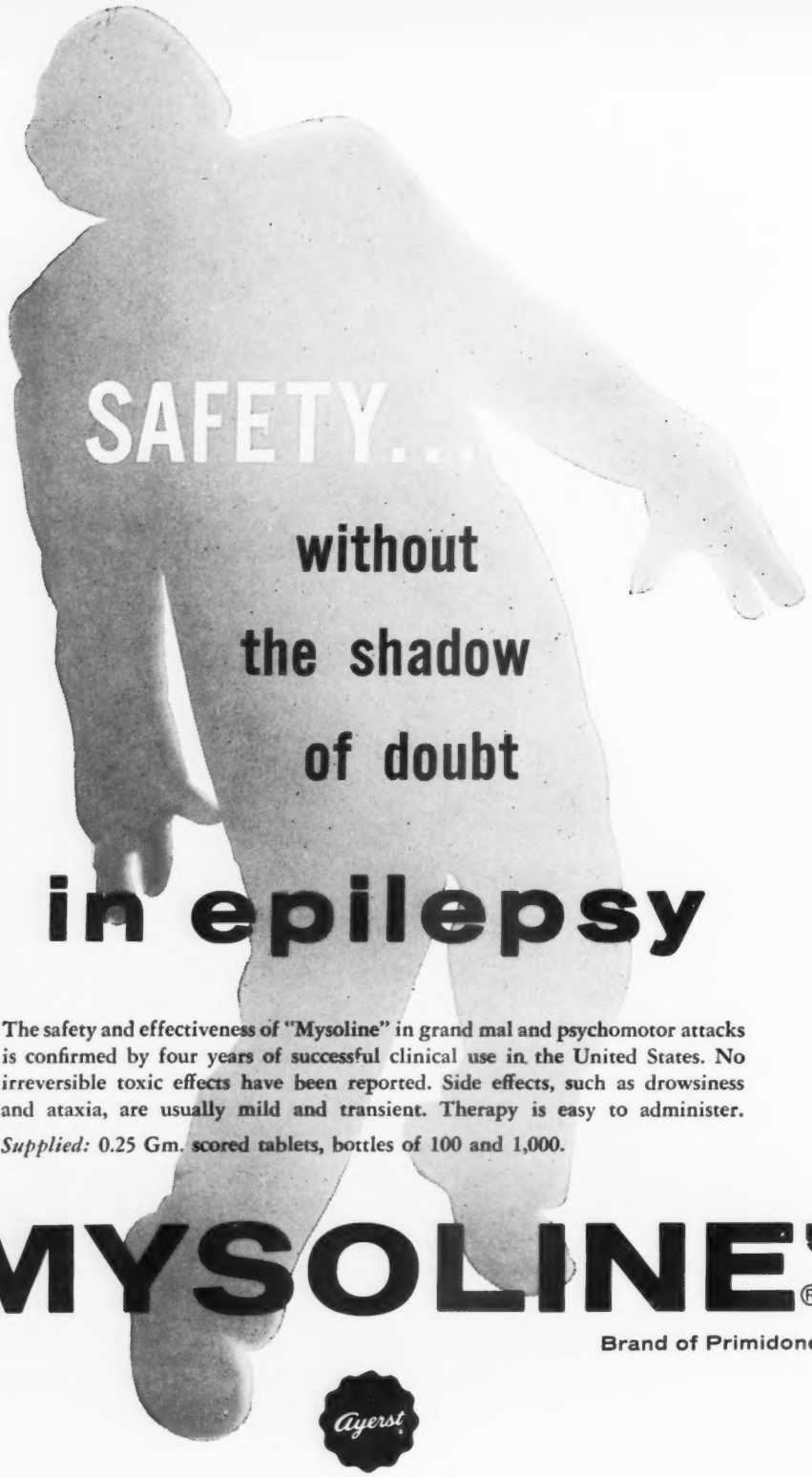

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References: 1. Vorbusch, H. J.: J. Clin. & Exper. Psychopath., (Jan.-Mar.) 1959
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1. Pennington, V.M.: The use of Deprol in chronic psychotic patients. Am. J. Psychiat. 115:250, Sept. 1958. **2.** Alexander, L.: Chemotherapy of depression—Use of meprobamate combined with benactyzine (2-diethylaminoethyl benzilate) hydrochloride. J.A.M.A. 166:1019, March 1, 1958. **3.** Settel, E.: Treatment of depression in the elderly with a meprobamate-benactyzine hydrochloride combination. Submitted for publication, 1958. **4.** Personal communications from physicians; in the files of Wallace Laboratories.

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DISEASES of the Nervous System

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

Differences on Measures of Self Concept

(College Students Referred to a Psychiatric Service and Classmates)

DANIEL H. FUNKENSTEIN, M.D., HENRY WECHSLER, PH.D., JOHN F. MERRIFIELD, A.B., and CHARLES C. MCARTHUR, PH.D.

In a monograph Funkenstein, King and Drolette[1] reported on a study of 125 Harvard College students. None were volunteers, being selected at random from the Junior Class. Each subject was studied during 20-30 sessions. Although the focus of the testing was the reaction of the students during laboratory stress-inducing situations, they also were given psychological tests and psychiatric interviews. In addition, sociological data were collected. Two aspects of stress reactions were delineated: the immediate acute emergency reactions of the subjects and the ability of the subjects to handle stress as time passed. The acute emergency reactions of the subjects were classified as follows: 1. No emotion—denial of emotional feelings; 2. Anger directed outward; 3. Anger directed inward toward the self; 4. Anxiety.

The psychological test results which correlated with the acute emergency reaction were not related to the ability to handle stress as time passed. The psychological factors which correlated with the ability to handle stress as time passed were not related to the acute emergency reactions. The acute emergency reactions and their correlates were termed the "basic disposition" of the individual, and the ability to handle stress as time passed was interpreted as a measure of "ego function," i.e., the adaptative function of the ego. Table 1.

Upon the basis of this work, the following hypothesis was stated: The acute emergency reaction and its correlates (basic disposition) represents the qualitative content of an emotional illness, should one develop, but proneness to develop such illnesses is related to an inability to master stress. With the completion of these laboratory studies it was decided to test this hypothesis in a college population. If an entire entering class of students could be tested at the time of matriculation, a comparison could be made in subsequent years between those who received psychiatric treatment in the University Health Services and their classmates who did not. These differences could be related to the test results obtained at the time they matriculated.

Due to limitation of time, only one test could be used. Accordingly, the Brownfain Concept of Self Test was chosen because one of its measures correlated with the Basic Disposition data in the previous research, and another of its measures correlated with

TABLE 1—*Correlates of the Two Phases of Laboratory Stress Reactions.*[4]

Personality Correlate	Basic Disposition	Ego Function
	Acute emergency phase	Ability to master or failure of mastery
Perception of parents	Significant	Random
Brownfain Internal Concept of Self	*Significant*	*Random*
Fantasies (T.A.T.)	Significant	Random
Social attitudes	Significant	Random
Social stratification	Significant	Random
Brownfain Social Conflict Index	*Random*	*Significant*
Assessment of reality	Random	Significant
Integration of personality	Random	Significant

From the Harvard University Health Service and the Department of Psychiatry, Harvard Medical School.

the Ego Function data. The specific hypotheses to be tested in this experiment were: The Brownfain Internal Concept of Self results, acquired at the time of matriculation of the students, would show no significant differences between the students subsequently seen in the University Health Service psychiatric department and their classmates (basic disposition); the Brownfain Social Conflict Index results would show significant differences between these same two groups of students, with the students seen in the University Health Service with psychiatric difficulties having higher scores on this measure than their classmates not seen in this service (ego function).

Method

Subjects: A class at an eastern private college, designated Class A, were administered the Brownfain Concept of Self Test in the fall of their freshman year, at the time of their matriculation physical examination which was given within nine weeks of the beginning of the academic year; 1055 students were tested; 9 refused to cooperate; 11 students failed to complete the tests.

The Brownfain Concept of Self Test: This test developed by Brownfain[1] measures the dynamic differences between the individual's conception of himself as seen from several different frames of reference. This is done by having the subject rate himself on 25 traits, using a scale of 1 through 8. Adequate definitions of the low and high end of the scale for each trait are provided. He is first asked to rate himself on these traits as he really thinks he is. Next, he is asked to rate himself again on the 25 traits, this time giving himself the benefit of any doubt and rating himself the highest that he thinks he is. The third time he is asked to rate himself on the traits at the lowest he thinks he is. Finally, he rates himself on these traits as he thinks others would rate him, that is, others in the group with whom he lives and works. Brownfain defined these four methods of rating as providing information about the "private self," "positive self," "negative self," and "social self."

Using the difference between pairs of ratings, Brownfain developed two measures. First was the 'stability of self concept," renamed by us the "internal concept of self," which was the sum of the differences between the positive self and the negative self ratings on each variable. Second was the sum of the differences between the private self and social self rating on each variable called the "Social Conflict Index." This Index thus measures the differences between the student's perception of himself and the way he feels that his peers perceive him.

The Psychiatric Cases: At the end of their freshman years in college for the class tested at the time of matriculation, the records of the University Health Service were examined for the men in this class who had been seen by a psychiatrist in the department and on whom a psychiatric diagnosis was made. These diagnoses were as follows: anxiety reactions, depressions, interpersonal problems, etc. These were then designated as Psychiatric Cases. Fifty students fulfilled these criteria for inclusion in this group; the other 1015 students tested were designated the Control Group.

Results: A comparison of the Control Cases and the Psychiatric Cases on the results of the Internal Concept of Self Measure of the Brownfain Test are shown in Table 2. The median of 50 for the entire class was chosen as the cutting point.

TABLE 2—*Internal Concept of Self Scores. Freshman Students (Class A) Tested at Matriculation Physical Examinations.*

	49 or less	50 or more
Controls	530 (52.2%)	485 (47.8%)
Psychiatric Cases	29 (58.0%)	21 (42.0%)
	Not significant	

The results on the same comparison between the Control Cases and the Psychiatric Cases on the scores of the Social Conflict Index are shown in Table 3. The cutting point chosen again was the median, in this case 20.

TABLE 3—*Social Conflict Index Scores of Freshman Students (Class A) Tested at Matriculation Physical Examinations.*

	19 or less	20 or more
Controls	579 (57%)	436 (43%)
Psychiatric Cases	16 (32%)	34 (68%)
	$x^2=12.12$	$p=.001$

Discussion

These results support the basic hypothesis. There was a significant difference in the Brownfain Social Conflict Index scores of the students who were subsequently seen in the University Psychiatric Service during their freshman year, as compared with their classmates. Both groups were tested at the time of their matriculation physical examinations, which was a considerable period of time before many consulted the psychiatric service. There were no significant differences between the Internal Concept of Self Brownfain scores of these two groups of students (Figure 1).

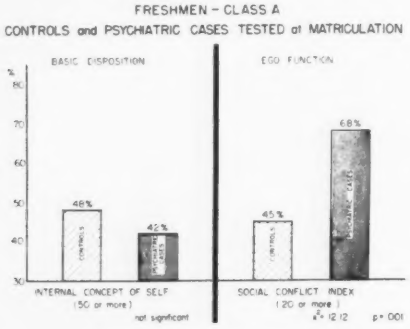

Figure 1. Comparisons on Brownfain Test of controls and psychiatric cases tested at time of matriculation. Class A.

These results can be stated in another frame of reference: the students who were subsequently seen in the University Psychiatric Service differed from their classmates on data interpreted as measuring ego function, but not on data interpreted as related to that aspect of personality termed the basic disposition.

A question of great interest which cannot be answered from the data we have is the following: Were the students with high scores on the Brownfain Test at the time of matriculation, and who were subsequently seen by a psychiatrist, already having psychological problems of sufficient magnitude to need help, or did they later develop such difficulties? The best method for studying this problem would be to retest the students at the time of their contact with the psychiatrist and compare these Brownfain results with the data obtained on them at the time of matriculation. Unfortunately, this was not done on a large scale but is planned for future research. We have retested three students from this class who have subsequently developed psychiatric difficulties, and in all three instances there is a change of great magnitude in their Social Conflict Index scores in the predicted direction but little change in their Internal Concept of Self scores.

On the basis of our original work,[4] another hypothesis stated that the Internal Concept of Self score (Basic Disposition) would be related to the type of psychiatric illness developed by an individual. In this study the number of psychiatric cases (50) was too small to test this hypothesis.

Of interest is data collected on another class of freshmen, designated as Class B of which 22 members were administered the Brownfain Test in the University Health Service at the time they were psychiatric patients. The results were compared with those obtained on a random sample of 132 of their classmates who had not been seen for psychiatric difficulties. The results of these comparisons may be seen in Table 4 and Table 5 (Figure 2).

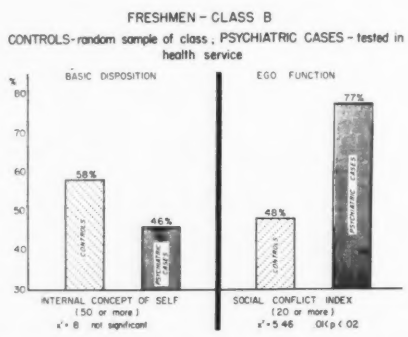

Figure 2. Comparisons on Brownfain Test of controls and psychiatric cases of Class B.

TABLE 4—*Internal Concept of Self Scores of Random Sample of Freshman Class B (Controls) and Group of Same Freshman Class Tested in University Psychiatric Service.*

	1-49	50 or more
Class B Freshmen Controls: (Random sample of Freshman class B)	55 (41.7%)	77 (58.3%)
Class B Freshmen Psychiatric Cases (Tested in Health Service)	12 (54.5%)	10 (45.5%)

x2=.8 Not significant

TABLE 5—*Social Conflict Index Scores of Random Sample of Freshman Class B (Controls) and Group of Same Freshman Class Tested in University Psychiatric Service.*

	1-19	20 or more
Class B Freshmen Controls: (Random sample of Freshman Class B)	69 (52.3%)	63 (47.7%)
Class B Freshmen Psychiatric Cases (Tested in Health Service)	5 (22.7%)	17 (77.3%)
$x2=5.46$	$.01 < p < .02$	

Still other data confirmatory of these same relationships was obtained on senior students, designated Class C, at the same college. The comparisons between the two Brownfain measures of a random sample of 92 seniors and a group of 25 seniors in this same class tested at the time they were patients in the psychiatric service of the University Health Service may be seen in Table 6 and Table 7 (Figure 3).

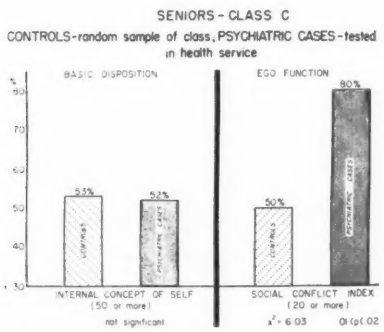

Figure 3. Comparisons on Brownfain Test of controls and psychiatric cases of Class C.

TABLE 6—*Internal Concept of Self Scores of Random Sample of Seniors, Class C (Controls) and Group of Same Senior Class Tested in University Psychiatric Service.*

	1-49	50 or more
Class B Senior Controls (Random sample of Senior Class C)	43 (47%)	49 (53%)
Class C Senior Psychiatric Cases (Tested in Health Service)	12 (48%)	13 (52%)
Not significant		

TABLE 7—*Social Conflict Index Scores of Random Sample of Senior Class C (Controls) and Group of Same Senior Class Tested in University Psychiatric Service.*

	19 or less	20 or more
Class C Senior Controls: (Random sample of Senior Class C)	46 (50%)	46 (50%)
Class C Senior Psychiatric Cases (Tested in Health Service)	5 (20%)	20 (80%)
$x2=6.03$	$.01 < p < .02$	

These results show that in three different comparisons using three totally different populations, a significant difference exists in each trial between the Social Conflict scores of students having emotional difficulties of sufficient magnitude to require psychiatric treatment and the controls. No significant difference was found in these groups on the Internal Concept of Self measure.

Interesting is the experimental design of this research. In the original studies,[4] a random sample of students was observed during actual laboratory stressful situations. These results were broadened in the research reported in this paper to include real life situations. The same measure of the Brownfain Test which correlated with the inability to handle stress in the laboratory correlated with the inability to handle the stresses of living; the other measure of the Brownfain Test which did not correlate with the ability to handle stress in the laboratory did not correlate with the ability to handle real life stresses.

The test results which correlated so highly with the ability to handle stress in time are measures of interpersonal perception. They measure the differences between the student's perception of himself in relation to his perception of what his peers think of him. This is the dimension of personality which Riesman[6] termed "other-directiveness," and which he finds so prevalent in American life. He states that modern youth is peer related and depends for his orientation and standards of behavior on his perceptions of his colleagues' expectations of him. Our data lend some support in this particular college culture to this thesis. The student who perceives a marked difference between his feelings about himself and his

perceptions of his colleagues' feelings about him is apt to have psychological difficulties of sufficient severity to bring him to the attention of the psychiatrist.

Our other data[3] indicate that students having difficulty in handling stress not only have discrepancies between their feelings about themselves in relation to their perception of their colleagues' feelings about them, but in actuality they are usually unable to perceive accurately their peers' feelings about them. The majority of students who mastered stress in the laboratory were able to perceive at a high degree of accuracy their roommates' ratings of them on a variety of psychological traits; those who had failed to master stress in the laboratory showed an inability to assess accurately their roommates' ratings of them on a variety of traits. One interpretation of these data is that students having difficulties in assessing reality have difficulties in mastering stress. Ability to act on the reality principle is related to ego function. Psychoanalytic theory lends support to this interpretation of the data.

Other data[3] suggest another dimension to interpersonal perceptions. We administered the Brownfain Test to a random sample at another college whose students differed markedly from the students whose test results are reported in this paper. This other college contained students who were in the great majority of instances highly mobile socially and the first members of their families to obtain a higher education. About all commuted to college. In the testing situation, the great majority of these students immediately asked questions about the meaning of the section of the Brownfain which instructs them to rate themselves as they feel their classmates would rate them. They stated that they had not thought much about this. "How would I know what my classmates think of me?" This question had never been asked by the students in the college where the original testing was done. Students in this latter college were in the majority of instances not so highly mobile socially—approximately 80 per cent of their fathers have college educations.

In further experiments, we found that the majority of students at the original college could repeat the Brownfain Test on different occasions without a significant change in their scores; the majority of students at the college with the very upwardly socially mobile students could not. The failure of students at this latter college to repeat the Brownfain with the same results was due to their inability to repeat accurately their rating of their perception of how their peers would rate them. These data suggest that the importance attached to interpersonal perceptions of one's peers (Other-directiveness), as well as skill in this area, may be related to social and cultural factors.

In this same area, other work of ours with the Brownfain Test is of interest. Nine students at the original college who had very poor academic records were tested; eight were unable to repeat the grading of their perceptions of classmates' ratings of them with any reliability. Interviews revealed that they thought very little about classmates' perceptions of them. This inability to perceive accurately their peers' perceptions of them or actually to correctly perceive their own performance is often found in students with poor academic records. Farnsworth, Funkenstein and Wedge[2] in their study of the Early Admission College Students, the so-called "Ford Scholars," described a group of students whose academic difficulties were ascribed to "Inappropriate Values for Education." They were always astounded and surprised when called to the dean's office and told that their work was unsatisfactory. In all instances, these students came from families with little education and were often the first members of their families to enter a university. Many came to a college in an urban environment from an extremely rural background. We would postulate that coming to college represented for these men a marked change in culture. If they came from a social or cultural background where interpersonal perceptions were not highly developed, they were unable to orient themselves in their new college culture. Hitson and Funkenstein[5] related skill in interpersonal relations to the child rearing practices of families.

This research raises more questions than it answers. The students upon whom the chief experimental work is reported in this

paper have three years of college remaining. They will be followed to see whether the same significant differences are found between those requiring psychiatric treatment and the controls. Some of those tested may have received psychiatric help on a private basis away from the health service and we have no means of identifying them. This research suggests many fruitful areas for future research and that the Brownfain Test is a reliable instrument for determining one aspect of psychological difficulties, i.e., perception of interpersonal relationships (ego function) in this particular college culture.

Summary

1. The Brownfain Concept of Self Test was administered to an entering class at an eastern private college at the time of their matriculation physical examinations. At the end of their freshman year, 50 of these men had been seen in the University Health Service by psychiatrists for psychological difficulties. The data obtained at the time of matriculation of these psychiatric cases were compared with data obtained on their classmates tested at the same time who were not subsequently seen in the University Health Service by a psychiatrist.

a. A significant difference was found between these two groups on the Social Conflict Index scores of the Brownfain. No significant differences were found between the Internal Concept of Self scores on the Brownfain of these two groups. On the basis of previous work, the Social Conflict Index (a measure of interpersonal perception) was interpreted as a measure of ego function, and the Internal Concept of Self (a measure of the perception of the self in two frames of reference) as a measure of the basic disposition.

b. The same results were found when two additional populations were studied: (1) A random sample of another freshman class in the same college designated controls were compared with psychiatric cases in their same class tested at the University Health Service. (2) A random sample of the senior class was compared with psychiatric cases in the same class tested at the University Health Service.

2. These experiments were planned to test the following hypotheses developed on the basis of previous work:[1] The Internal Concept of Self Measure (Basic Disposition) would show no significant differences between the students seen in the Health Service and their classmates; a significant difference would be found between these same two groups on the Social Conflict Index Measures (Ego Function). Although the data collected supported the basic hypothesis, it did not allow us to answer the question of whether high scores on the Social Conflict Index indicated that the student was prone to develop psychiatric difficulties or whether he already was having such difficulties at the time he was tested.

3. The implications of this research were discussed from two standpoints: Laboratory-stress experiments and Riesman's "other-directiveness" of today's college youth.

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BIBLIOGRAPHY

1. Brownfain, J. J.: Stability of the Self-Concept As a Dimension of Personality. *J. Abnormal & Social Psychol.*, 47:597 (1952).
2. Farnsworth, D. L., Funkenstein, D. H., and Wedge, B.: A Study of the Social and Emotional Adjustment of Early Admission Students. *Fund for Advancement of Education*, New York, 1956.
3. Funkenstein, D. H.: Unpublished Data.
4. Funkenstein, D. H., King, S. H., and Drolette, M.: Mastery of Stress. *Harvard University Press*, Cambridge, 1957.
5. Hitson, H., and Funkenstein, D. H.: Patterning in Families of Depressed and Paranoid Patients (*In preparation*).
6. Riesman, D.: The Lonely Crowd. *Yale University Press*, New Haven. 1952.

Seizures in Neurosyphilis

GREGORY S. FERRISS, M.D.

Introduction

The data presented here were collected in an attempt to find the incidence and any distinguishing characteristics of seizures occurring in patients with neurosyphilis. There are three large series of cases in the American literature. Incidence of convulsive seizures in patients with neurosyphilis at the Boston Psychopathic Hospital has been reported as 20% by Greenblatt and Levin.[1] Among 151 paretics, 35 (23%) had seizures. Merritt, Adams and Solomon[2] give a 14% incidence of convulsions in 42 patients with cerebral vascular lues at the Boston City Hospital. Gillen and Moossy found convulsions in 20% of 100 paretics at Charity Hospital in New Orleans. These are summarized, together with the author's cases, in Table VIII.

Method

At the Charity Hospital of Louisiana at New Orleans, records on neurosyphilitic inpatients in the 6 years from 1949 through 1955 were examined. Standards for the diagnosis included a positive spinal fluid and blood complement fixation reaction. The date of the lumbar puncture which yielded the positive spinal fluid reaction was taken as of the date of diagnosis. All cases were new; previously diagnosed cases with exacerbations or relapses were excluded. Many cases were rejected and not included in this series because of insufficient recorded clinical information for classification as to type of neurosyphilis, lack of laboratory data, and other reasons. Cases were classified as follows:

Paresis (parenchymatous cerebral, encephalitic, G.P.I. etc.) in which symptoms and signs were mainly those of cerebral involvement.

Meningo-vascular lues, in which predominant symptoms and signs were of meningitis or a recognizable vascular syndrome. The distinction from parenchymal lues was not always clear. In some cases, though the admission incident was a vascular syndrome, if there was strong evidence of more general involvement such as dementia or bilateral Babinski signs, the classification assigned was paresis.

Tabes dorsalis, in which spinal root and cord were involved. Optic atrophy alone was also included in this group.

Tabo-paresis, in which there was evidence of both spinal and cerebral parenchymal involvement.

Asymptomatic, in which the only evidence of syphilis was in blood and spinal fluid reactions. Asymptomatic cases with non-reactive pupils as the sole sign have been included here.

Asymptomatic-except-for-seizures is a category made to include two cases in which such was the case.

Results

There were 165 cases of definitely diagnosed neurosyphilis among in-patients during the years 1949 through 1954. These cases were divided into two groups: 1) with seizures, and 2) without seizures. Of the 165, 35 (21%) had seizures (Table 1). The age distribution is indicated in Table II. The sex distribution is shown in Table III. The

TABLE I

Incidence of Cases of Neurosyphilis by Year of Diagnosis

	1949	'50	'51	'52	'53	'54	Total
With seizures	8	4	2	10	3	8	35
Without seizures	17	23	17	24	19	29	130
Total	25	27	19	34	22	37	165

TABLE II

Distribution of Cases of Neurosyphilis by Age (Decade)

	2nd	3rd	4th	5th	6th	7th	8th	Total
With seizures	2	1	11	8	7	5	1	35
Without seizures	3	3	17	37	38	21	11	130
Total	5	4	28	45	45	26	12	165

TABLE III

Incidence of Cases of Neurosyphilis by Sex

	Male	Female	Total
With seizures	26	9	35
Without seizures	82	48	130
Total	108	57	165

From the Department of Psychiatry and Neurology, Louisiana State University School of Medicine, New Orleans, Louisiana.

TABLE IV

Distribution of Cases by Type of Neurosyphilis

	Paresis	Meningo vascular	Tabo-paresis	Tabes	Asymp-tomatic	Other	Total
With seizures	23a	7	3	0	0	2d	35
Without seizures	43a	37	8b	22	18c	1e	130
Total	66	45	11	22	18	3	165
Percent. of total cases in series	40	27	7	13	11	2	100

a. Includes 2 cases of congenital syphilis-juvenile paresis.
b. Includes 1 case with features of tabes and vascular occlusion.
c. Includes 1 case of congenital syphilis.
d. Asymptomatic except for seizures.
e. Amyotrophy and cervical pachymeningitis.

TABLE V

Incidence of Seizure Types in Cases of Neurosyphilis

	Paresis	M-V	T-P	Asymptom-atic except for seizures	Total
Grand Mal only	13	1	2	1	17
Focal (motor)	6	5	0	1	12
Focal (psychomotor)	2	0	0	0	2
Focal & Grand Mal	2	1	1	0	4
Total	23	7	3	2	35

distribution of cases by type of neurosyphilis is indicated in Table IV. The types of seizures encountered are shown in Table V.

Of the 35 cases with seizures nine were paretic, six meningo-vascular, and two asymptomatic-except-for-seizures. Seizures were the presenting symptom in all but one of the meningo-vascular cases with seizures.

Examples of Cases of Meningo-vascular Syphilis with Seizures

Case S7: J.D., 75 year old colored male, had a single left focal motor seizure on the day of admission. Examination showed transient left hemiparesis. C.S.F. protein 112 mgs%, 1111000000, K & K positive (blood serology positive 32 units). Diagnosis (5/7/54): Meningo-vascular lues. Treatment: 13.2 million units penicillin. Course: Readmitted one month after discharge with similar seizures, which were controlled easily with Dilantin and phenobarbital.

Case S16: O.J., 67 year old colored male, suddenly became comatose, soon having right focal motor seizures. Examination showed status epilepticus for two days, with a seizure every 10-15 minutes. CSF protein 130 mgs%, 5555555432, K & K positive (blood serology positive 16 units). Diagnosis (12/9/54): Meningo-vascular lues. Treatment with penicillin was begun. Course: death after 9 days, no autopsy.

Case S26: L.V., 42 year old colored male, began having left-focal motor seizures 4 days P.T.A. Examination showed slight left hemiparesis. CSF: 0 cells, protein 83 mgs%, 4433321000, VDRL and Kolmer positive (blood serology positive). EEG: Right temporo-parietal slow focus. Diagnosis (11/10/50): Meningo-vascular lues. Treatment: 16 million units penicillin. Course: Asymptomatic at discharge.

Cases Asymptomatic-neurosyphilis-except-for-seizures

Case S13: W.I., 49 year old colored male, began having generalized seizures 9 months P.T.A. Examination was normal. CSF: 0 cells, protein 72 mgs%, 4441110000, K & K positive (blood serology positive 128 pnits). EEG was normal. Diagnosis (5/6/52): Neurosyphilis, asymptomatic-except-for-seizures. Treatment: Aureomycin 60 grams, phenobarbital and Dilantin. Course: Seizures controlled. CSF (11/13/52): 2 cells, 3332210000, K & K positive (blood serology positive 16 units).

Case S30: I.W., 56 year old colored male, began having right focal motor seizures 5 years P.T.A. Examination was normal. CSF: 5 lymphs, protein 36 mgs%, 3332210000, K & K positive. (Blood serology positive). EEG showed spikes and a slow focus in the left temporal region. Diagnosis: Neurosyphilis, asymptomatic-except-for-seizures. Treatment: 11.2 million units penicillin; phenobarbital. Course: Seizures controlled on discharge.

Cases With Seizures and Death

Case S29: E.W., 52 year old colored female, suffered a "stroke" 2 years P.T.A. She became confused one week P.T.A. Examination showed an organic mental syndrome. CSF: 3 cells, protein 84 mgs%, 5555532100, K & K positive (blood serology positive 512 units). EEG was generally slow. Diagnosis (2/18/52): Paresis. Treatment was begun with penicillin and aureomycin. Course: Patient had two seizures, focal in onset, the first two weeks later. Secondary bronchopneumonia and other infectious complications contributed to death.

Case S15: M.F., 60 ycar old colored female, complained of weakness and giddiness for one week followed by coma 1 day P.T.A. Examination showed generalized convulsions and coma. CSF: protein 98 mgs%, 5555421000, K & K positive. (Blood serology positive.) Diagnosis (9/10/49): Meningovascular lues. Treatment with penicillin was begun. Course: Patient died three days after diagnosis. No autopsy.

Case S16: (See above).

Examples of Cases With No Further Seizures On No Anticonvulsants

Case S28: A.A., 35 year old white male, had several sudden alterations in consciousness preceded by dizziness for several weeks P.T.A. Automatic repetitious motor activity and/or tonic rigidity were described. Examination showed hyperactive reflexes and bilateral Babinski signs. CSF: 190 lymphocytes, protein 122 mgs%, 5555543100, K & K positive (blood serology positive). EEG during treatment was normal. Diagnosis (9/22/50): Paresis. Treatment: 9.4 million units penicillin. Course: Recovery. C.S.F. (6/14/51): 0 cells, 1112100000, Kolmer positive. No seizures in two years.

Case S20: A.M., 54 year old colored female, showed progressive mental deterioration for 6 months P.T.A. and 2 right Jacksonian seizures the day P.T.A. Examination showed an organic mental syndrome and right hemiparesis. CSF: protein 76 mgs%, 444432100, K & K positive. (Blood serology positive 64 units). Diagnosis (4/3/53): Paresis. Treatment: 12 million units penicillin. Course: No further seizures; general improvement until 10/5/54, when she experienced a sudden left hemiplegia, probably embolic from a previously demonstrated myocardial infarction. CSF (10/9/54): 8 polys, 2 lymphs, protein 86 mgs%, K & K positive. Re-treatment with same dosage. Continued improvement.

Thirteen cases have been inadequately followed or lost; 14 continue to have seizures at various levels of control.

Examples of Treated Cases With Continuing Seizures

Case S22: J.R., 58 year old colored male, had gradually progressive mental deterioration and psychomotor seizures for 3 years P.T.A. Examination showed an organic mental syndrome. CSF: 12 lymphs, 2 polys, protein 64 mgs%, 44443210000, K & K positive (blood serology positive). EEG showed a right anterior and mid-temporal slow focus. Diagnosis (10/17/52: Paresis. Treatment: 7.2 million units penicillin. Course: Patient showed psychotic behavior following treatment. Seven months later he was given 4 EST, immediately after which he went into status epilepticus and phenobarbital. CSF (6/3/53): 1 lymph, protein 55%, 5555531000, K & K positive. He was given 18.6 million units of penicillin. On anticonvulsants, generalized seizures gradually decreased from one per month to one in six months, and mental status improved greatly.

Case S9: L.G., 44 year old colored male, noted memory impairment for two months. Examination showed recent memory loss and disorientation for time. CSF: 2 polys, 1 lymph, protein 70 mgs%, 555543210, K & K positive (blood serology was 64 units). Diagnosis (8/19/53): Paresis. Treatment: 12 million units penicillin. Course: Improvement in mental status was gradual. 4 months later patient had first of two generalized convulsions. These were completely controlled on small doses of phenobarbital, and the mental status returned to normal.

In 30 of the cases with seizures, the seizures preceded the establishment of a diagnosis. In four cases seizures occurred first during treatment. In only one case (S9, see above) did seizures start after treatment.

Five cases with seizures were included in the group of cases without seizures because the seizures were not clearly related to neurosyphilis, though they may have been.

Cases in Which Seizures Were Probably Not Related to Neurosyphilis

Case 48: 17 year old colored male was mentally retarded, having achieved 6th grade at age 16. For one year he had been lethargic, for 6 months confined to bed, and shortly prior to admission, stuporous and incontinent. Examination showed flexion deformities in the right extremities, dementia, with dissociated emotional responses. No stigmata of congenital syphilis were found. CSF: 10 lymphs, protein 71 mgs%, 5554421100, K & K positive (blood serology 512 units). EEG was normal. Diagnosis (2/8/51): Juvenile paresis. (His mother's serology was positive). Treatment: 10 million units of penicillin, 60 gm. of aureomycin (over a one month period). Course: There was gradual steady improvement. CSF: (1/18/52): Protein 52 mgs%, 5555210000, K & K positive. On 4/5/53, patient was in the hospital for re-evaluation. There is a note that he had a "convulsion," fell out of bed, and fractured his humerus. This is the only mention of seizures in the whole record.

Case 54: E.J., 58 year colored male, had received hip and arm shots 13 years P.T.A. He was admitted with urinary retention, and examination showed absent reflexes in the lower extremities (blood serology positive). Diagnosis (1/6/51): Tabes dorsalis and luetic aortic aneurysm. Treatment: 10 million units of penicillin. Course: No progression of neurological signs. He had an excision of the aortic aneurysm on 3/27/53, and a note in this history mentions "falling1out spells" for the previous 6-7 months. These were interpreted as episodes of vascular insufficiency rather than seizures. CSF (4/2/54): 3 lymphs, protein 45 mgs% 0001000000, K & K positive.

Case 71: G.P., 60 year old colored male presented with mental confusion. CSF: 11 lymphs, protein 51 mgs%, 4444321100, K & K positive. (Blood serology 16 units.) Diagnosis (12/6/52): Paresis. Pulmonary tuberculosis and chronic alcoholism were also found. Treatment: 7 million units of penicillin. Course: Patient was readmitted in 4 months with far-advanced pulmonary tuberculosis. He had a generalized seizure the day after admission. He was re-treated with 10.8 million units of penicillin and placed on phenobarbital, gr. ½, q.i.d. He remained in the hospital for 10 months because dementia made outpatient care impossible. Six days after discharge he was readmitted in status epilepticus. CSF (1/19/54): 2 lymphs, 1 poly, protein 41 mgs% 5555543210, K & K

positive. On regaining consciousness a right hemiparesis was found. No further seizures occurred until discharge.

Case 130: T.R., 49 year old white male, had gradually progressive intellectual impairment, distractibility, and hypersexuality progressing to profound confusion over 11 months. Examination showed an organic mental syndrome with frontal lobe features. CSF: 33 lymphs, protein 68 mgs%, 55554431000, K & K positive (blood serology 8 units). EEG was generally slow. Diagnosis (7/19/54): Paresis. Treatment: 15 million units of penicillin. No follow-up. In this case there was a history of 5 seizures during the patient's lifetime, one in childhood and the others associated with alcohol. There had been no seizures during the development of the paresis.

Case 131: T.S., 40 year old white female, suddenly became comatose. Examination showed, in addition, a right hemiparesis. CSF: Protein 77 mgs%, 5555554321, K & K positive (blood serology positive). Diagnosis (12/21/52): Meningovascular lues. Treatment: 43 million units of penicillin. In the history, epileptic seizures since the age of nine were mentioned but not described in further detail. Blood serology had been negative on routine test on 11/24/47.

It is of interest to note that in the 45 meningovascular cases without seizures, there were 5 (11%) brain stem syndromes (2 Weber, 2 Wallenberg, 1 Raymond).

It was found that treatment of neurosyphilis varied greatly, reflecting the divergent attitudes of physicians of the many hospital services that managed these cases. In most cases where penicillin was used alone, more than 10,000,000 units were given, usually divided over a 7-14 day period. Excluding asymptomatic cases or those who died during treatment, of those cases receiving penicillin alone, 19 cases received less than 9.6 million units (this figure was chosen because it was the dosage recommended by the Louisiana State Department of Health as the minimum dosage for treatment of asymptomatic neurosyphilis during most of the included years); 14 of these cases had inadequate follow-up. Three patients who received less than 9.6 million units showed reversion of spinal fluid findings toward normal, though they did not necessarily improve clinically.

Cases With Serologic Improvement on Less Than Usually Recommended Treatment

Case 82: E.B., 39 year old colored female who had received undetermined amount of treatment for lues in 1948, had spells of weakness for 3 years, and generalized and left focal motor seizures for 3 months. Examination showed a left hemiparesis. CSF: 5 cells, protein 52 mgs%, 555432100, K & K positive (blood serology positive). Diagnosis (3/14/49): Meningovascular lues. Treatment: 6 million units penicillin. Course: 6 months later, CSF (10/5/49): protein 35 mgs% 1122100000, K & K negative (blood serology weakly positive). There were no further seizures until 20 months later, when she was readmitted, having been in focal status for 2 weeks. CSF (12/28/50): 8 lymphs, protein 57 mgs%, 544-2100000, Kolmer negative, Kline positive. She was given a further 12 million units.

Case 810: B.G., 35 year old colored female, had sudden onset of status epilepticus. Examination after control showed mild organic dementia which persisted a week. CSF: 480 cells (88% lymphs, 12% polys), protein 134 mgs%, 5555421100, K & K positive (blood serology positive). Diagnosis (6/13/49): meningovascular lues, luetic meningitis, luetic heart disease. Treatment: 5 million units. Course: Seizures continued infrequently and no anticonvulsants were taken. CSF (5/1/51): 15 lymphs, protein 28 mgs%, 5521100000, K & K positive. (2/2/52): 2 lymphs, protein 31 mgs%, 4442221100, K & K positive. Patient had frequent seizures early in 1952, followed by persistent dementia; 12 million units of penicillin were given.

Case 822: (See above).

Case 819: V.L., 53 year old colored female, had sudden onset of a right hemiparesis and mild aphasia 1 year P.T.A. An organic dementia developed. A right adversive seizure precipitated her admission to the hospital. On admission she was agitated, demented and hemiparetic. CSF: 5 lymphs, protein 68 mgs%, 112310000, K & K positive (blood serology positive). Diagnosis (6/4/49): Paresis and diabetes mellitus. Treatment: 5.9 million units penicillin in one week. Course: There were no further seizures. CSF (1/28/51): 3 lymphs, protein 43 mgs%, 1112200000, Kline negative, Kolmer weakly positive. (Blood VDRL doubtful, Kahn 1.)

Case 828: (See above).

Two cases on treatment with 7.2 million units of penicillin became worse and required retreatment.

An occasional case showed progression following supposedly adequate treatment. The possibility of re-infection is strong.

Example of a Case Showing Progression Following Treatment

Case 128: 56 year old colored female who had a strongly positive blood serology in 1930 ,age 29), but she had no treatment until 1951. Examination showed a sociopathic personality, cirrhosis and effects of alcohol CSF: Protein 18 mgs%, 2222110000. Diagnosis (2/22/51): Asymptomatic neurosyphilis. Treatment: 12 million units penicillin over 16 days. Course: She was readmitted 5 years later with a

right hemiparesis and dementia which had set on gradually over the years. CSF (3/19/56): 4 polys, 2 lymphs, protein 120 mgs%, 4444432100, K & K positive. She was retreated with 5 million units of penicillin and improved clinically.

It is of incidental interest to mention that several cases received treatment other than penicillin. Five cases received aureomycin and penicillin, with satisfactory results. One elderly tabetic was treated with potassium iodide alone. A young tabetic was arrested following malaria alone.

Electroshock treatments were used in several paretics following definitive treatment. The variation in use and dosage of anticonvulsants in the cases with seizures was too wide for any conclusions.

Comments

This series of cases cannot be taken as representative of the actual number of cases of neurosyphilis in the community. This would undoubtedly be found much higher. During the included years Louisiana ranked among the first ten states in the nation in mortality due to paresis, among the first five states in first admissions to mental hospitals for all psychoses due to syphilis. Louisiana has been first in the nation consistently for a decade in mortality due to syphilis of all varieties. In 1956-7, house to house blood testing in Orleans Parish in selected lower economic housing areas yielded 4221 positive serological reactions (and 986 questionable) among a total of 40,611 tests. The figures available from the Louisiana State Health Department are given in Tables VI-VII; however, these figures probably give only a rough estimate of incidence, probably lower than the actual incidence. Some factors accounting for this discrepancy should be mentioned. At the largest public health venereal disease clinic in New Orleans, less than one-quarter of all the patients with positive blood reaction submit to lumbar puncture and spinal fluid examination. It is the policy of the clinic to advise that lumbar puncture be done, and if the patient refuses, penicillin in dosage considered adequate for treatment of neurosyphilis is given. In selecting in-patient cases for this series, many records were rejected because of incompleteness or failure to meet the requirement that the diagnosis be made for the first time in the included years. Many cases of neurosyphilis were excluded because of this. Some idea of the in-patient hospital cases is given by the record librarian's statistics: the total number of discharge diagnoses of various forms of neurosyphilis during the year 7/53-7/54 was 149, and during 7/54-7/55 was 167. Multiple admissions and several diagnoses were probably included on a few patients, thus making the actual number of cases less; however, it is almost certain that there were several times the number of in-patient cases during the included years than could be included in this series. Many other cases were diagnosed and treated in the out-patient department, and no statistics are available on these.

Because of the above factors it is felt that a detailed comparison of symptoms, signs etc. with other series of such cases as that of Merritt *et al.*, would not be worthwhile or meaningful. With respect to percentage seizure incidence, however, this series agrees closely with the other three mentioned in the introduction. The overall percentage incidence is in close agreement with Greenblatt and Levin. Other differences can be noted in Table VIII. One of the greatest factors accounting for these is probably the necessity of making a diagnosis of type of neurosyphilis from chart information, especially differentiating meningovascular from parenchymal cerebral syphilis.

All main types of seizures are seen in neurosyphilis. (See Table V.) Realizing the limitations imposed by seizure descriptions,

TABLE VI

Luetic Morbidity, U.S.A. and Louisiana, 1949-1954

(Louisiana State Health Department)

	Syphilis, All Types			Late & Late Latent		
Year	U.S.	Louisiana	La./U.S.%	U.S.	Louisiana	La./U.S.%
1949	288736	10278	3.5	135862	5386	4.0
1950	229723	9535	4.2	119343	5109	4.3
1951	198640	8570	4.3	115284	4894	4.3
1952	168734	7925	4.7	109138	5494	5.0
1953	156099	8247	5.3	106240	6394	6.0
1954	137876	5277	3.8	97955	3685	3.8

it would be unjustified to say more than that generalized and focal motor seizures are probably most frequent. As might be expected, it would seem that focal motor seizures are more prominent in meningovascular lues than in the other types of neurosyphilis.

At the East Louisiana State Hospital, a large state mental hospital, the present population of paretics is 310. 119 of these cases were admitted during the years 1949-1954. (A few of the included Charity Hospital cases were transferred to this institution.) The incidence of seizures among this group is 24 cases (8%). This percentage incidence is much less than in the above described Charity cases. Though it is not known how many of these patients had seizures at the time of original diagnosis, the noted difference in incidence would reinforce the evidence that seizures disappear after definitive antiluetic treatment in many paretics, and occur only infrequently as a late sequel.

In reviewing the cases, one is struck by the number of potentially preventable cases. Often the diagnosis of syphilis was made many years previously, but treatment was not carried out. Often symptoms were present for years before medical attention was sought. Despite the great advances in therapeutics and public health case-finding, neurosyphilis in this area continues to be an important medical problem.

TABLE VII

Deaths From Syphilis in Louisiana, 1949-1954

(Louisiana State Health Department)

Year	All Syphilis Total	Rate/100,000	Paresis	Tabes	Other CNS Syphilis	Syphilis Unqualified
1949	279	10.5	35	3	33	22
1950	260	9.7	32	2	26	23
1951	219	8.1	35		16	5
1952	184	6.6	19	1	23	9
1953	201	7.2	24		10	22
1954	184	6.5	22		10	7

TABLE VIII

	Number of Cases				Seizures	
	Paresis	M-V	Tabo-P	Total	Number	Percent
Greenblatt & Levin	151				35	23
		25			9	36
				223	44	20
Gillen & Moossy	100				20	20
Merritt, Adams and Solomon		80			14	17.5
Ferriss (Charity)	66				22	33
		45			7	16
			11		3	27
				165	35	21
(E. La. State Hosp.)	310				24	8

Summary

Data are presented on neurosyphilitic inpatients at Charity Hospital of Louisiana at New Orleans in the years 1949 through 1954. Of 165 cases, 35 had seizures as part of their illness. In Table VIII these cases are compared with other series, with which there is substantial agreement. Other aspects of the problem of neurosyphilis are briefly mentioned.

REFERENCES

1. Greenblatt, M., and Levin, S.: Neurosyphilis, Convulsions and Electroencephalography. *Urologic and Cutaneous Review,* 50: 331, 1946.
2. Merritt, H. H., Adams, R. D., and Solomon, H. C.: Neurosyphilis. *Oxford University Press,* New York, 1946.
3. Gillen, M. W., and Moossy, J.: A Survey of the Clinical Features of Paresis. *Bull. of Tulane Med. Fac.,* 2: 17, 1951.
4. Martin, J. D.: Venereal Disease Statistical Letter. Issue No. 1, *La. State Department of Health,* March 1957.

Basic Studies in Mongolism

I. Serum Proteins

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Chemical studies on mongolism have generally indicated no significant differences between the mongoloid patient and the control. Some interesting observations that have been reported however, are elevated serum lipid levels[1] and lipoproteins[10] as well as impaired absorption of vitamin A in oil.[11] Hypocalcemia has also been noted. The urinary excretion of β-aminoisobutyric acid, a catabolic product of nucleoprotein metabolism, is elevated in mongolism.[13] It has been suggested that the ability to excrete this metabolite is under genetic influence.[2,4] In view of these findings associated with mongolism, the present study was undertaken to determine if any differences exist in the proteins, glycoproteins and free amino acids in the serum of mongoloids as compared to controls.

Procedure

The subjects were chosen from individuals in all age brackets who showed obvious mongoloid stigmata. The controls consisted of two groups who were matched for age and sex as nearly as possible with the experimental group. This matching should serve to control variables of diet, environment and activity. The first group of controls were non-mongoloid mentally retarded patients from the same ward. It is possible that this latter group would have a characteristic metabolic pattern of their own. For this reason a second control group of normal individuals was included. Eighty-nine patients with mongolism and sixty controls in two groups were used in the investigation.

Electrophoretic Technique:

This procedure is based on the property of protein molecules, at a pH other than their isoelectric point, of migrating toward an electrode when they are suspended in an appropriate medium and a potential is applied to the system. The rate of migration is dependent principally upon the net charge of the individual protein moiety.

Fractionation of proteins by this method is the result of varying migration rates for constituents of the mixture. Serum proteins subjected to this procedure typically separate into five fractions at pH 8.6. These are albumin, alpha$_1$-globulin, alpha$_2$-globulin, beta-globulin, and gamma-globulin. Of these, albumin has the fastest migration rate (mobility) and the others follow in the order given.

In brief, the method of paper electrophoresis employed in this study is carried out by spotting a protein sample (serum) onto a strip of filter paper which is saturated with buffer solution (Veronal buffer at pH 8.6, ionic strength 0.075). A constant current (9 mamp.) is then applied across the paper strips for a period of 16 hours, and during this time, separation of the protein fractions occurs along the length of the strip. The strip is dyed with bromphenol blue, and the relative proportions of the separated fractions are estimated on the basis of the amount of dye absorbed, each fraction being expressed as a percentage of the total protein. This quantitative estimation was carried out on a Spinco Analytrol.

The following determinations were made on the experimental and control groups:

(a) In 16 mongoloids and 17 mentally retarded controls the polysaccharide constituents (glycoproteins) of the electrophoretically separated serum protein fractions were examined by a modified Schiff-periodic acid reaction.[9]

(b) Duplicate electrophoretic determinations of serum proteins were made for all subjects by the technique described above.

(c) Sera from 35 mongoloids and an equal number of mentally retarded controls have been analyzed qualitatively for free amino acids by means of duplicate two-dimensional chromatograms, using 77% ethanol as phase I solvent and water-saturated phenol as phase II solvent. A ninhydrin (0.5%) spray was used for color development.

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TABLE I

% Polysaccharide Contained in Serum Protein Fractions

(Rounded off to nearest whole number)

Subject	*Albumin*	*Alpha$_1$ Globulin*	*Alpha$_2$ Globulin*	*Beta Globulin*	*Gamma Globulin*
Control	12.0 (SD 4.0)	13.0 (SD 3.0)	26.0 (SD 6.0)	25.0 (SD 4.0)	24.0 (SD 5.0)
Mongoloid	8.0 (SD 4.0)	13.0 (SD 3.0)	29.0 (SD 4.0)	24.0 (SD 4.0)	26.0 (SD 7.0)

TABLE II

Serum Protein Distribution

(Values expressed as % of total serum protein)

Subject	*Age Group*		*Albumin*	*Alpha$_1$ Globulin*	*Alpha$_2$ Globulin*	*Beta Globulin*	*Gamma Globulin*
Controls (normal)	17.8—26.8	(11)*	51.5 † (SD 5.7)	4.4 (SD 0.7)	10.6 (SD 3.2)	18.2 (SD 4.1)	15.3 (SD 2.5)
Controls (mentally retarded)	3.3— 9.2	(9)	55.6 (SD 1.6)	4.4 (SD 0.8)	11.9 (SD 2.7)	12.7 (SR 1.7)	15.4 (SD 2.7)
	15.1—33.6	(31)	52.9 (SD 5.4)	5.1 (SD 1.1)	10.4 (SD 2.2)	12.7 (SD 1.9)	18.9 (SD 3.3)
	50.7—70.6	(3)	52.9 (SD 0.96)	5.4 (SD 0.2)	11.1 (SD 0.6)	12.2 (SD 2.3)	18.2 (SD 3.8)
Mongoloid	1.3— 2.9	(11)	51.7 (SD 6.4)	4.2 (SD 0.96)	16.2 (SD 3.7)	12.5 (SD 2.1)	15.4 (SD 2.8)
	3.0— 9.2	(24)	52.4 (SD 4.8)	4.7 (SD 0.8)	12.2 (SD 2.8)	12.5 (SD 1.8)	18.2 (SD 4.0)
	10.3—39.4	(39)	48.2 (SD 5.9)	4.6 (SD 1.1)	11.3 (SD 2.5)	12.8 (SD 2.1)	23.1 (SD 5.1)
	41.1—63.6	(7)	46.3 (SD 3.6)	5.2 (SD 1.1)	11.8 (SD 2.1)	12.8 (SD 1.1)	23.9 (SD 3.5)

* Number in parenthesis indicates subjects in that group.

† Standard deviation.

TABLE III

*Summary—Serum Proteins in Mongolism**

(Values expressed as % of total protein)

Investigator	*(Ref.)*	*Subjects*	*Albumin*	*Alpha$_2$ Globulin*	*Alpha$_1$ Globulin*	*Beta Globulin*	*Gamma Globulin*
Horvath	(5)	25	51.1	2.5	8.9	12.2	25.9
Stern et al.	(12)	36	48.3	6.1	10.9	13.1	21.7
Sobel et al.	(11)	18	45.8	5.8	10.6	13.7	23.9
Carver et al.		39	48.2	4.6	11.3	12.8	23.1

*Age differences not taken into consideration.

Results

Table I indicates the results obtained in the study of the serum glycoproteins. The differences noted are not statistically significant.

In presenting the data on the serum protein profile, the subjects have been divided into groups on the basis of age. It should be emphasized that this is an arbitrary division. Table II indicates the three groups studied as well as the number of subjects in each group and the serum protein profile. The concentration of gamma globulin is elevated in serum of mongoloids when compared to mentally retarded and normal controls. This difference in the concentration is statistically significant (P .001). In contrast to the results of Sobel, et al.,[11] the differences in albumin concentration were not found to be statistically significant, although an appreciable difference does exist.

Subjective comparison of the chromatograms of the free amino acids of the serum were essentially the same in the experimental and control groups. Moreover, no significant differences were noted in the total serum proteins between the groups. The mongoloid group, however, tended to be lower.

Discussion

Independently, three other groups of investigators have arrived at similar conclusions in studying the plasma protein profile. Table 3 summarizes the data from these authors. The present study, however, contained a much larger patient group than the others, as well as having a sizeable number of older mongoloids and mentally retarded patients included. Small differences in staining and scanning techniques have an appreciable effect on serum electrophoretic studies and it is necessary to be critical in evaluating results from different laboratories. It would appear from Table III that the elevation in concentration of the gamma globulin and decrease in concentration of albumin has been adequately established; in fact, the results are quite consistent between the laboratories.

Very little information is available on the causes of hyper-gammaglobulinemia; it appears to be principally the result of antigenic stimulation, infection or hypersensitivity reactions, hepatic disease, or neoplasms containing gamma-globulin producing cells.[6] According to Janeway and Gitlin "it seems reasonable to assume that an appreciable increase in the concentration of gamma-globulins in the blood reflects their increase synthesis, whether the rate of removal by loss or catabolism is normal or increased."

The explanation for the elevated gamma globulin in these studies is not apparent. Sobel[11] offers no explanation while Stern[12] comments on the resemblance to aftermath of chronic infections, suboptimal liver function and possibly leukemia. The possibility that albumin to gamma globulin ratio is under genetic influences[7,8] would be an interesting point for speculation on the above results. Additional information on the properties of the gamma globulin from mongoloids is needed before an explanation can be adequately offered.

The results indicate that the gamma globulin in mongoloids increases with age; a similar situation is true for the non-mongoloid mentally retarded patient but to a lesser degree. The high gamma globulin has not been noted in newborn mongoloids.[3,11] The tendency towards an increase becomes apparent prior to age 10 and appears to become more prominent with advancing age. The significance of this finding is not known. It may reflect an early injury to the reticuloendothelial system or genetic factors may be involved.

Summary

Investigations on 89 mongoloid and 60 controls have indicated an elevated serum gamma globulin. This finding is statistically significant. Serum glycoprotein and serum free amino acids comparative studies showed no significant differences in the groups studied.

REFERENCES

1. Benda, C. E., and Mann, G. V.: The Serum Cholesterol and Lipoprotein Levels in Mongolism. *J. Pediat.*, 46:49-53, 1955.
2. Calchi-Novati, C., Cellellini, R., Blancho, I., Silvestroni, E., and Harris, H.: β-aminoisobutyric Acid Excretion in Urine. A Family Study in an Italian Population. *Ann. Eugenics*, 18:335-336, 1954.
3. Carver, M. J.: Unpublished Observations.
4. Harris, H.: Family Studies on the Urinary Excretion of β-aminoisobutyric Acid. *Ann. Eugenics*, 18:43-49, 1953.
5. Horvath, L.: Down-betegek serumanak vizsgalata papirelektroforesissel. *Orvosi Hetilap*, 42: 1166, 1955.
6. Janeway, C. A., and Gitlin, D.: Advs. in Pediatrics 1957. *Interscience Publishers, Inc.*, New York, N. Y.
7. Lewis, L. A., and Page, I. H.: Heredity Obesity: Relation to Serum Lipoproteins and Protein Concentration in Swine. *Circulation*, 14:55-59, 1956.
8. Page, I. H., Lewis, L. A., and Gilbert, J.: Plasma Lipids and Proteins in Their Relationship to Coronary Disease Among Navajo Indians. *Circulation*, 13:675-679, 1956.
9. Roboz, E., Hess, W. C., Forster, F. M.: Determination of Serum Proteins and Polysaccharides. *Arch. Neurol. and Psychiat.*, 73:536-543, 1955.
10. Simon, A., Ludwig, C., Gofman, J., and Crook, G. H.: Metabolic Studies in Mongolism. *Am. J. Psychiat.*, 111:139-145, 1954.
11. Sobel, A. E., Straggrella, M. A., Sherman, B. S., Elkan, B., Morgenstein, S. W., Marius, N., and Meisel, A.: Vitamin A Absorption and Other Blood Composition Studies in Mongolism. *Am. J. Ment. Def.*, 62:642-656, 1958.
12. Stern, J., and Lewis, W. H. P.: Serum Proteins in Mongolism. *J. Ment. Sci.*, 103:222-226, 1957.
13. Wright, S. W., and Fink, K.: Excretion of β-aminoisobutyric Acid in Normal, Mongoloid and Non-Mongoloid Children. *Am. J. Ment. Def.*, 61: 530-533, 1957.

Mode of Action of Rauwolfia Derivatives in Schizophrenic States (A Psychodynamic Formulation)

H. AZIMA, M.D., and FERN J. AZIMA, M.A.

The purpose of this communication is to present certain observations in support of the hypothesis that rauwolfia therapy in schizophrenic states produces what appears to be a shift in certain respects from a schizophrenic organization towards a manic-depressive organization.

Method

Observations were made in two series of schizophrenics: chronic and acute. The chronic schizophrenic group consisted of 20 female patients with an average age of 45 and an average duration of hospitalization of 10 years. They were seen for a period of one week prior to pharmacotherapy for the assessment of the psychodynamics and then received reserpine for 6 weeks (6-10 mgm daily), placebo for 4 weeks and raudixin for 6 weeks (6-10 gm daily). The emergent psychodynamic changes were investigated through twice weekly interviews, and independent psychological testings (Rorschach and Figure Drawing) before, after reserpine period and after raudixin period.

The acute schizophrenic group consisted of 10 patients, 5 male and 5 female, with an average age of 35. They were seen for 10 days prior to, for 6 weeks during, and for 10 days after pharmacotherapy, 2 to 3 times weekly. Psychological explorations were based on psychoanalytic principles. The aim of the sessions was not solely therapeutic but the recording of emergent changes or events in the psychodynamic field regardless of the direction of changes. The major coordinates of changes were mood, ego defenses, drives and object-relationship.

Observations

These have been reported partly elsewhere[1,2] and will be presented in summary here. Due to the relative consistency of certain fiindings in both schizophrenic groups and the psychological test data, the findings will be combined. Changes were noted in the following areas:

1. *Mood Organization.*

In chronic schizophrenics the major alterations of mood appeared to be: (a) a relative increase in overt anxiety in 12 cases, confirmed in 7 out of 11 cases by psychological tests; (b) the appearance of a manic-depressive mood change in 13 patients. Three developed a hypomanic and two manic reactions. In two patients a mild depression followed the manic phase. Overtly a feeling of elation was expressed by eight other patients. In psychological tests feelings of elation were noted in 10 out of 11 patients with the first drug period. The manic state in the two patients did not appear to be either a "turbulent phase" or a catatonic agitation. Our impression was based on the experential state of acceleration, elation and overactivity.[1]

In acute schizophrenics in general the mood underwent three phases: indifference in six of the cases; mania of elation in eight of the cases; depression in four of the cases. The indifference was noted particularly in patients with persecutory anxieties, as a distancing between ego and hallucinated voices ("the voices don't bother about killing me"); ("I feel I have no energy . . . there is a kind of solidness between the voices and me," etc.) The manic phase was expressed as elation by eight patients, in three of whom a hypomanic state was manifest ("I am in a hurry within myself"; "I feel exhalted, I mean in good humor, etc."). The phase of depression when present always followed the manic phase.

2. *Ego Organization.*

In chronic schizophrenics there appeared a relative increase in ego strength in 16 out of 20 cases under pharmacotherapy manifested in a better reality contact, a decrease in projection, withdrawal, and splitting. Psychological tests confirmed this impression in

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10 out of 11 cases investigated with the first and in nine in the second drug period. The decrease in the defenses of withdrawal and splitting appeared to result in an emergence of impulses and a picture of a decrease in control. This was apparent clinically in 13 cases, two of which showed a manic state—and in Rorschach of six patients with the first and of seven patients in the second drug trial (decrease in form, increase in anxiety indices, greater color responsivity, etc.)

The changes in the defense of splitting was particularly noted in three acute schizophrenics, in the form of a change in the feeling of being in bits and pieces to the feeling of wholeness.

3. *Drive Organization.*

The changes in schizophrenic defense system appeared to have resulted in an emergence of drives, particularly aggression. In chronic schizophrenics this was evident in the overt behavior of three patients, and in delusions of six other patients. Genital impulses emerged in three patients. No decrease in destructive tendencies was detected by the psychological tests. Aggressive indices showed an increase in seven out of 11 cases with the first and in five with the second drug trial. The emergent needs were, in general, of either oral or anal nature.

In acute schizophrenics the emergence of aggression was observed in overt behavior of two patients, in dreams of two patients, and in figure drawings of two patients.

Discussion and Conclusions

The above mentioned observations, which are the outline of detailed psychodynamic explorations of a relatively small number of patients within a relatively short period of time, indicate that rauwolfia administration seems to result in: (1) a change in schizophrenic defenses of withdrawal, splitting and projection; (2) a change in drives, mainly aggressive impulses; (3) a change in mood, roughly in a sequence of indifference, mania and depression. It should be emphasized that our main concern was with emergent alterations. In our opinion there is some certainty that these appeared independent of alteration due to transference phenomena. In no case was the schizophrenic structure fundamentally altered, and only in one case all the changes previously mentioned were present (The typical case). With these reservations in mind, what was noted under rauwolfia administration could be conceptualized as a partial shift from schizophrenic to manic-depressive.

The pathogenesis of this shift is a matter of speculation. In a psychoanalytic frame of reference we feel that the primary influence of rauwolfia can be attributed either to an alteration in sources of drives or to an alteration of psychic intensity or cathecting energy of the mind, which is a resultant of the former. We find this hypothesis useful because both sources of drives and cathecting energy are processes proximate to organicity and it is more understandable to envisage a chemical substance affecting an organically proximal state than psychological states, such as defenses. Besides, there is some evidence to indicate that rauwolfia derivatives influence diencephalic neuronal sets which are related to the sources of certain drives.

The drive most likely disturbed in its sources and in its cathexis, according to the present data, seems to be aggression. This is understandable if we consider the importance of the vicissitude of aggressive drives in manic-depressive states. Additional confirmation for this contention is the frequency of depression in hypertensive patients treated with rauwolfia. Various studies indicate the importance and the role of aggression in hypertension.

Considering that in several cases there was an initial state of indifference particularly in regard to the persecutory images, and noting the importance of super-ego in manic-depressive states, it is consistent to say that the agency of the mind affected mostly by the shift in the cathexis was super-ego system (internalized reality controlling system or image percepts). Finally it may be said that the released destructive impulses were more effective against a partially decathected and de-invested super-ego system. And this mechanism, i.e. destructive rejection of super-ego is assumed in present psychoanalytic conceptions to be an important mechanism of manic organization.

Thus, through these speculations, it seems possible to relate the observations noted in this study, and make the suggestion that perhaps one modality of action of rauwolfia derivatives in schizophrenic states is the initiation of a shift toward a more organized state, with a more structured ego system of manic-depressive organization.

Authors' Note: Rauwolfia preparations used were rau-sed (reserpine) and raudixin (whole root) kindly supplied by E. R. Squibb & Sons.

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BIBLIOGRAPHY

1. Azima, H., Cramer-Azima, Fern J., and DeVerteuil, R.: A Comparative Behavioral and Psychodynamic Study of Reserpine and Equally Potent Doses of Raudixin in Schizophrenics. *Monographs on Therapy,* Vol. 1, No. 2, 15-25, 1956.
2. *Ibid.*: Effects of Rauwolfia Derivatives on Psychodynamic Structure. Presented at the American Psychiatric Association Meeting, Chicago, May 15th, 1957.

Fluphenazine: A Preliminary Study

HARRY F. DARLING, M.D.

Fluphenazine, the complete chemical formula of which is 4(-[3-2-(trifluoromethyl)-10-phenothiazyl] propyl)-1-piperazine-ethanol, dihydrochloride, a phenothiazine derivative, is the trifluoromethyl homologue of perphenazine. Pharmacological studies would seem to indicate that it is approximately 25 times as potent as chlorpromazine, and that in cats, dogs, and monkeys its side effects are essentially the same on a weight-dose basis as the trifluoromethyl homologues of prochlorperazine and thiopropazate.[1] This medication was given to 110 female patients at the Danvers State Hospital for a period of four or more months, except in some instances where it was discontinued due to side effects. All degrees of chronicity and behavior are represented in the study. Table 1 classifies the patients by duration of illness as determined by their social histories. Table 2 gives the diagnoses of the group. Table 3 classifies the patients by chronological age.

Table 4 shows dosage. Initial doses were increased until improvement was found or discontinuation made necessary due to side effects. Dosage was increased every day or two, or in the very high doses, once or twice a week. Estimation of initial dose was made by evaluating the severity of the psychosis and the physical condition of the patient. In the first few weeks of the study there was a tendency to be a little too high, particularly as initial action is often extremely rapid; the patients had to be observed closely for reactions.

Injectible doses in patients who refused oral medication were as follows:

1.25 mg. daily in four aged patients;

1.25 mg. four times daily and then 2.5 mg. every four hours in two patients having extreme catatonic excitement and in two very high manics;

2.5 mg. three times daily in one excited catatonic, and four times daily in another.

In the case of one of the elderly patients neurocirculatory collapse occurred after the third dose; she recovered, but due to her age the medication was not reinstituted. Improvement was moderate to marked in two or three days in these patients and oral medication could be instituted, except that one of the aged patients took four days to improve to the point that she would take the medicine orally.

Probably the best starting dose for the younger psychotic is between 5 mg. and 10 mg. daily, and between 2 mg. and 5 mg. in the elderly. Increases should be made cautiously as the drug is extremely potent. In many cases it would seem that the drug is as much as twice as potent as estimated experimentally, which could equate it to 50 times the potency of chlorpromazine in certain cases. Its average dosage seems about half that reported for trifluoperazine in similar cases.[5,8,9]

Improvement is shown in Table 5. Patients who went home or had ground parole are indicated in this table only from the psychotic

From Danvers State Hospital, Hathorne, Massachusetts.

TABLE 1

Duration in years	Percentage of patients
1–0	20.9
1–2	11.8
2–5	22.7
5+	44.5

TABLE 2

Diagnosis	Percentage of patients
Schizophrenia	53.6
Mental deficnency with psychosis	13.6
Chronic brain syndrome	13.6
Manic-depressive	6.3
Personality disorder	5.4
Psychoneurosis	4.5
Involutional reaction	1.8
Paranoid condition	0.9

TABLE 3

Age	Percentage of patients
16–20	3.6
21–25	1.8
26–30	10.0
31–35	4.5
36–40	8.2
41–45	12.7
46-50	7.3
51–55	10.0
56–60	10.0
60–65	10.9
66 +	20.8

TABLE 4

DOSAGE BY PERCENTAGE OF PATIENTS

Mg./day	Initial	Maintenance
1	0	1.8
2	2.7	1.8
2.5	7.3	10.9
3	1.8	1.8
5	17.3	29.1
7.5	16.5	13.6
10	16.5	14.6
15	20.9	10.9
20	4.5	3.6
30	6.4	3.6
40	0.9	1.8
60	1.8	2.7
75	0.0	0.9
80	0.9	0.9
100	1.8	0.9
180	0.0	0.9

TABLE 5

IMPROVEMENT BY PERCENTAGE OF PATIENTS

Home or paroled	10.9
Marked	15.5
Moderate	34.5
Minimal	15.5
None	23.6

groups. The non-psychotics were graded as to improvement by whatever change in their subjective symptoms and behavior was evident. Among the patients who showed no improvement are included those who were taken off the drug due to side effects.

Both in new and long hospitalized patients the drug was effective. In new patients it was to be expected that a phenothiazine derivative would be effective but the results were better than expected in the chronics. More patients could be continued on this drug than could on its chemical progenitor, perphenazine, as seen in a previous study.[2] In the perphenazine cases the side effects, although similar, come more often before clinical effectiveness is reached. Most of the perphenazine cases were chronic disturbed patients, however, and the basis of comparison is not completely valid because, although many of the patients receiving fluphenazine were chronics, not too many were disturbed. A study is under way on the use of the new drug in chronic disturbed patients and the comparative results in this respect should be more valid. Of the patients in this study that were chronically disturbed, however, the results were good and the majority could be kept on the drug at dosage levels that maintained their improvement.

Side effects are indicated in Table 6. Extrapyramidal effects occurred at all dosage levels, even the lowest. The patient on 180 mg. daily showed not only no side effects but little overall improvement on this drug or on other drugs she has taken. Parkinsonism in many cases was controllable by cutting the dose and/or adding antiparkinsonian agents. Probably there would have been a few less such cases if, early in the work on the drug, smaller starting doses had been used. Ten patients (9.1%) had to be discontinued due to severe parkinsonism.

The lethargic cases, some of them verging on the stuporous, were all controlled by diminishing the dose. As in some of the parkinsonian cases, this manifestation occurred early and was due to a too high initial doses. A couple of patients took their first 2.5 mg. dose and became so lethargic and tranquilized that they did not move out of bed for several hours but they did not become stuporous. Their psyches changed almost im-

TABLE 6

PERCENTAGE OF SIDE EFFECTS

Parkinsonism	31.8
Lethargy	9.1
Depression	7.3
Akathisia	7.3
Equilibrium disturbance	3.6
Neurocirculatory collapse	3.6
Leukopenia	3.6
Propulsion	1.8
Edema	1.8
Jaw Spasms	1.8
Abdominal spasms	0.9
Polyuria	0.9
Blurring of vision	0.9
Myoclonic movements of orbicularis oris	.09
Rash	0.9
Nasal congestion	0.9
Flushing	0.9

mediately and they lay there with blissful, relaxed expressions on their faces; they were acute schizophrenics, not violent.

All but one of the depressed patients had to be taken off the drug. With the exception of two acute cases, they were chronic schizophrenics.

Five of the akathesia cases had to be discontinued; the other three were controlled with methane sulfonate or procyclidine hydrochloride.

Three of the equilibrium disturbances were controlled by reduction of dosage. The other, complicated with severe parkinsonism, had to be discontinued.

With the exception of the aged patient mentioned above the drug could be continued in the cases that had neurocirculatory collapse.

Two of the leukopenias were temporary, taken off the drug a week, and then reinstituted without further trouble. The other two were taken off permanently because of their extreme age and infirmity; it was not thought wise to gamble with their tenuous hold on life. They were put on thiopropazate and maintained their improvement without leukopenia.

One case of edema was facial and in the other both face and hands were edematous. Both responded to antihistaminics.

One propulsion case was temporary, had no other extrapyramidal symptoms, and responded to reduction in dosage. The other is described below.

Two of the three spasm cases were controlled by methane sulfonate and the third by reducing the dose to half and adding ten times the amount of trifluprom azine. This measure, by the way, was attempted in other extrapyramidal manifestations and was successful in about a third of the cases. The cases put on the combination were counted in this study among those taken off the drug due to side effects.

The polyuria cases did not improve, nor did the one with myoclonic movements, but they could be continued on the drug. The rash case had to be discontinued. The cases that had flushing, stuffy nose, and blurring of vision were temporary.

Of those cases in which the dose was reduced due to side effects, only those were kept on the drug who continued to improve.

Among the cases that had multiple side effects the most interesting was the one that had equilibrium loss, akathisia and parkinsonism on 10 mg. daily, and another that had lethargy, propulsion and nasal congestion on 5 mg. Two cases had akathisia with parkinsonism and two had parkinsonism and lethargy. There was one case of each of the following: depression and akathisia, depression and lethargy, edema and parkinsonism, parkinsonism and vasomotor collapse, parkinsonism and depression, edema and neurocirculatory collapse, lethargy and flushing, parkinsonism with equilibrium loss, parkinsonism and rash.

Discussion

On the basis of 110 patients studied only a preliminary evaluation of a drug can be made. Further studies are under way at Danvers State Hospital and elsewhere. Although more akathisia and depression were noted with this drug than with perphenazine[2] the percentage of these two side effects is not particularly high. Akathisia particularly was not nearly as high as that noted at Danvers by the writer and coworkers[6] with trifluoperazine. Other studies agree.[3,4,7] So far parkinsonism seems less of a bugaboo with this drug than with perphenazine; higher therapeutic levels can be attained and maintained.

Phenothiazines are all useful. This medication is particularly valuable since it does

not produce akathisia to the extent of some of the other piperazine-phenothiazines, nor does it flatten affect especially. In this respect it is useful in both acute and chronic cases.[4]

Fluphenazine in its effects is predominantly sympathicolytic. The few vagolytic side effects appear to be those rare manifestations of reversal of effect that can occur with any drug.

Summary and Conclusions

1. Fluphenazine was used in 110 hospitalized patients and appears to be an effective antipsychotic agent for both acute and chronic cases. It is particularly advantageous in that it does not ordinarily produce any excessive flattening of affect, nor does it produce any great amount of akathisia.

2. In most patients adequate therapeutic dosages may be given and in some cases these doses have been very high. The use of the injectible form has been fast and effective. Extrapyramidal symptoms are frequent but are controllable in most cases without lowering the dose below therapeutic effectiveness, or by using antiparkinsonian agents, or both.

3. Patients who became depressed on this drug could not be maintained on it ordinarily.

4. Leukopenia does occur.

5. The drug is sympathicolytic in action.

6. Therapeutic effectiveness, milligram per milligram, is at least 25 times that of chlorpromazine, or even more.

REFERENCES

1. Burke, J. C., Linegar, C. R., and others: Pharmacology and toxicology of SQ4889, 4918 and 4924. N. J., *Squibb Institute for Medical Research.* (Laboratory reference manual) 1957.
2. Darling, H. F.: Use of Perphenazine in 100 Hospitalized Patients. *Dis. Nerv. System,* 19:10, Oct. 1958.
3. Feldman, P. E.: Evaluation of trifluoperazine in Chronic Schizophrenia. (In Trifluoperazine, Clinical and Pharmacological Aspects). Phila., *Lea & Febiger,* 1958, pp. 87-97.
4. Freyhan, F.: Occurrence and Management of Extrapyramidal Syndromes in Psychiatric Treatment With Trifluoperazine. *Ibid.,* pp. 195-205.
5. Haworth, K. W.: Preliminary Investigation of Prifluoperazine in Psychotic States. *Ibid.,* pp. 120-124.
6. Kruse, W.: Trifluoperazine in Chronic and Semichronic Schizophrenia. *Ibid.,* pp. 138-143.
7. Kovitz, B.: Management of Psychotic Tension Symptoms with Trifluoperazine. *Ibid.,* pp. 144-149.
8. Pollack, B.: Clinical Evaluation of Trifluoperazine. *Ibid.,* pp. 113-119.
9. Rudy, L. H., and others: The Use of Trifluoperazine in the Treatment of Acute and Chronic Psychotic Patients. *Ibid.,* pp. 125-137.

Author's Note: The fluphenazine used in this study was supplied by the E. R. Squibb & Sons under the trade name Prolixine.

The laboratory work in this study was done under the supervision of Evelyn Fisk, M.D.

National Society for Crippled Children and Adults, 2023 W. Ogden Ave., Chicago 12, Ill.

Metherdine as an Adjuvant to Electro-Convulsive Therapy

CHARLES Z. K. MITIS, M.D., and MARCELINO AMAYA, M.D.

The stimulus for this study came from the work of Fabing,[3] who several years ago introduced a modification of electroconvulsive therapy by giving patients a chemical cerebral stimulant shortly before a treatment. He used for this purpose Coramine, and after seven years of experience with it[4] arrived at the conclusion that it was the treatment of choice in acute mania and other forms of a psychotic excitement, which are not improved by electroshock alone. He explained this clinical observation on the basis of Pavlov's theory of production of the ultra paradoxical phase of cortical activity.

There is other evidence in the literature demonstrating that if a cerebral stimulant is given prior to ECT it will in some degree alter the results. Kleinschmidt[5] has shown that Benzedrine among others can lower the convulsive threshold in electric and azazol shocks and attributed this mainly to its central action on the subcortical centers, especially the hypothalamus, apart from protecting adrenalin from destruction by amino-oxidase. Andren[1] obtained better therapeutic results in ECT of depressed patients by administration of Meratran before the treatment. Lennox, et al.[6] have found that if Benzedrine is given to monkeys before an electrical shock, the electroencephalogram during and after the convulsions was somewhat altered in the majority of the animals so treated, and the animals appeared to be more alert afterward.

In this work methamphetamine hydrochloride (Methedrine) has been chosen as an adjuvant to ECT. This drug was selected for its very potent stimulating effect on the central nervous system, which has been shown by Levine, et al.,[7] Brussel, et al.,[2] and a number of other authors. In contrast to amphetamine, its central effect is much stronger, and its sympathomimetic (peripheral vascular) less potent.[7] The use of methamphetamine as an adjuvant to psychotherapy, to psychiatric diagnosis, and also as an antidepressant and stimulant is now generally accepted. It has been agreed by all authors that the increase of psychomotor activity, illustrated by free-flow of speech with a highly increased emotional charge, is the main psychological change. This together with the physiologic changes produced by methamphetamine would indicate its effect on the cortex, subcortical centers, especially hypothalamus and the endocrine system.

Method

A random sample of 50 female patients from one section of the hospital was selected for this study. They consisted of patients admitted in a consecutive order, in whom ECT was the chief therapy ordered. Every alternate patient was assigned to the study or control group, each numbering 25 patients. Except for premedications with Methedrine in the study group, the treatment was given in a very similar way. The physicians in charge of every case, who ordered and terminated the course of treatment, did not know which of the patients was receiving Methedrine. All patients were free from any serious physical abnormalities contraindicating ECT. A special emphasis was placed on the condition of the cardiovascular system; only four cases of mild essential hypertension and three cases showing some EKG evidence of a myocardial ischemia, but without a clinical evidence of impairment, were admitted to this study. The ages varied from 26 to 71 years in the study group, the average being 46.6; in the control group from 25 to 68, with an average of 48.3.

Table I, among other things, gives the diagnoses. In the diagnostic terms the 'standard nomenclature" of the American Psychiatric Association[9] was used. Severe overt anxiety was present in the majority of cases, but only six patients were actually classified as agitated. All patients classified as agitated were depressed. Two of them were included in the psychotic depressive reaction, and four in the category of involutional psy-

chosis. This is emphasized especially in connection with Fabing's observations.

In the electrical shock current of 550 ma/AC was applied for 0.6 to 1.5 seconds. All patients received premedications of atropine 1.2 milligrams subcutaneously, one-half to one hour before treatment. Occasionally a mild barbiturate sedative (Seconal 0.1 to 0.2 gm.) was given orally one hour before treatment, but this did not differ to any significant degree in the two groups. Blood pressure and pulse rate were taken on initial examinations after admission, and again before atropine was given, immediately before an electrical shock, and immediately after the convulsions. In the study group, Methedrine was given intravenously in dosage of 10 or 20 milligrams (0.5 to 1.0 cc) 15 to 25 minutes before the electrical shock. However, on some occasions, for various technical reasons, the time was extended up to 50 minutes, or shortened to five minutes. Not all of the patients received the same dose of Methedrine on every occasion. Thirteen patients were given 10 mg. at the beginning of the course of treatment, and this was later on increased to 20 mg. Seven patients were premedicated with 10 mg. before every treatment, and five with 20 mg. before each treatment. All patients received succinylcholine chloride immediately before the treatment.

The time of awakening after the treatment was measured and estimated by their ability to respond to verbal stimulus. Attempts were also made to estimate the degree of mental (organic type) confusion after each treatment, and generally during a whole course, and afterwards. This, however, was based on the clinical observation of various observers and may not have been too reliable.

The therapeutic results were estimated as poor, improved, or very good by the patients' physicians. Only short-term results, namely, the condition of the patients on dismissal from the hospital are given in Table I.

In the control group 246 treatments were given with an average of 9.84 per patient, and a total of 195 in the study group, with an average of 7.8 treatments per patient. The average number of treatments in a sample of 100 female patients treated recently with ECT in the same hospital was 9.97

Results

TABLE I

METHEDRINE GROUP

Diagnosis	No. Cases	Aver. EST's	Therapeutic Results: Poor	Fairly Good	Very Good
Manic depressive psychosis, depressed type	2	10	–	1	1
Manic depressive psychosis, manic type	0	–	–	–	–
Manic depressive reaction	7	7.1	1	3	3
Involutional psychotic reaction	6	6.6	–	2	4
Schizophrenic reaction, schizo-affective type	6	8	1	3	2
Schizophrenic reaction, paranoid type	2	8.5	–	1	1
Schizophrenic reaction, chronic undifferentiated type	1	14	1	–	–
Depressive reaction	1	7	–	–	1
Total	25	7.8	3	10	12

CONTROL GROUP

Manic depressive psychosis, depressed type	1	11	–	–	1
Manic depressive psychosis, manic type	1	13	–	1	–
Psychotic depressive reaction	9	9.1	1	5	3
Involutional psychotic reaction	6	9	–	3	3
Schizophrenic reaction, schizo-affective type	4	10	2	2	–
Schizophrenic reaction, paranoid type	2	12	1	1	–
Schizophrenic reaction, chronic undifferentiated type	0	–	–	–	–
Depressive reaction	2	11	1	–	1
Total	25	9.8	5	12	8

treatments per patient. The results of treatment, as illustrated on the table, were somewhat better in the Methedrine group, and this was even more apparent in some cases, whose brief histories will be quoted later.

There was no striking difference in the immediate post ECT confusion in the two groups. The time of awakening after the treatment varied within more or less the same limits in the two groups, and no definite conclusions could be drawn from the actual gures. Also, no definite difference in this respect was observed in those patients who received 10 or 20 milligrams of Meth-

edrine on various occasions. However, once awake the patients to whom Methedrine was administered appeared to be more alert and more active for several hours following the treatment, and never slept for two or three hours, as the controls often did. Some of the patients in the Methedrine group, especially in the early stages of the course of treatment, appeared to be even overactive for several hours after the treatment, and required additional sedation at night. This overactivity was never severe enough to interfere with the management of the patient. The overall organic impairment during the course of treatment and afterwards was estimated as lesser than in the controls by the majority of the clinical observers.

Case Histories

Case No. 1: Mrs. D.F.L., a 35 year old housewife, was hospitalized in this hospital about five years before for paranoid schizophrenia. She received four deep insulin comas and nine electrical shocks. She was dimissed only very slightly improved. She did very poorly outside the hospital, and was admitted again about a year later, to one of the state hospitals. She received a longer course of electrical shocks with some improvement. Following her dismissal from the state hospital she still suffered periodically from anxiety, psychophysiologic symptoms, and periodically would verbalize paranoid delusions. She was readmitted to this hospital in a state of acute exacerbation of all her symptoms, which include severe anxiety and agitation. The diagnosis was again schizophrenic reaction, paranoid type. She received six electrical shock treatments, in which 10 mg. of Methedrine was used as an adjuvant. The treatments were spaced within a twelve day period. She had no other treatment, except for sedatives, during the initial period of her stay in the hospital. There was practically no organic type of impairment present following the treatment, and there was an almost complete remission of her symptoms. A report received two months later from her husband stated that she was "better than he had ever known her before."

Case No. 2: Mrs. F.B., a 25 year old housewife, with a past history indicating an emotionally unstable personality, developed symptoms of a psychotic depressive reaction following a head injury. She sustained bruises and lacerations, but did not lose consciousness. When admitted to this rospital five months later there was no evidence of any organic abnormality. The EEG and skull x-ray were normal. She had a two inch linear scar on her forehead which was not disfiguring. Her symptoms consisted of insomnia, anorexia, loss of interest, and extreme irritability, with crying spells and temper tantrums. Most of the time she would appear to be very depressed, and expressed feelings of despondency and futility. She made two suicidal attempts, one by taking an overdose of sedatives, and the other by trying to jump out of the window. Psychological testing confirmed the diagnosis of depression and also revealed marked emotional instability and passive-aggressive traits in the patient's character structure. This was labeled by the examining psychologists as "a basically hysterical character." Soon after her admission she made another suicidal attempt, and shortly thereafter was placed on electroconvulsive therapy, with 10 mg. of Methedrine as an adjuvant to each treatment. The treatments were given on alternate dates, and she received a total of six. After the second treatment she exhibited a change in attitude; she became very sociable and cheerful, and two weeks later was dismissed in a state of a complete remission, without any clinical signs of an organic defect due to ECT. Unfortunately, there was no follow-up on this patient.

Case No. 3: Mrs. M.E.F., a 36 year old housewife, was admitted to this hospital for the first time in 1950, with a diagnosis of a post-partum schizophrenic reaction. At the time her main symptoms consisted of extreme anxiety, obsessive thoughts that something might happen to her husband and her children, depressed mood and paranoid delusions. She was treated with deep insulin therapy and electrical shocks. She was considered only slightly improved on dismissal, but apparently made a fair social adjustment, until about five years later, when she was again admitted to this hospital with a diagnosis of a schizophrenic reaction, schizo-affective type. Her symptoms were essentially the same as during her previous admission. This time there was no definite precipitating factor, and the onset was rather insidious. Again, she was treated with deep insulin therapy, combined with electrical shocks, and received 18 one-hour comas, and six EST's. She was improved on dismissal. The third (present) episode occurred 18 months later, and had a more acute onset. It coincided in time with a disagreement with her mother over some financial matters. The symptomatology again was similar, and the diagnosis was schizophrenic reaction, schizo-affective type. On this admission the treatment consisted mainly of a course of eleven electrical shocks, which were spaced within four weeks time; 10 mg of Methedrine was used as a premedication in the first four treatments, and 20 mg. in the remaining ones. Following the course of treatment, the patient had some memory defect, but this was so slight that she was able to leave the hospital two days after her last treatment. During the follow-up examination five months later, she was still asymptomatic.

These case histories were selected chiefly for the reason that the prognosis in these cases appeared to be poor or doubtful, and the actual therapeutic results were surprisingly good.

Side Effects and Complications

The side-effects were few, and none of them of any definite clinical significance. As was previously mentioned, a proportion of the patients who received Methedrine had increased psychomotor activity, and occasionally insomnia following treatment. This, however, was never a problem, and could be easily managed by additional sedation. To our surprise, the injection of Methedrine did not appreciably increase the patient's anxiety and fear of the electrical shock treatment. Only one patient, on her first treatment, became acutely disturbed and panicky after she received 20 mg. of Methedrine. In order to control her agitation she was given .25 gm. sodium amytal intravenously, which calmed her sufficiently to allow us to complete the treatment. In contrast to this, the majority of patients with a diagnosis of depression felt better after receiving Methedrine, and even looked forward to it.

The side-effects related to the cardiovascular system were only of a minor clinical importance. The basic blood pressure of patients in the study group varied from 105/64 to 160/94, the average being 127/80. The respective figures in the control group were 102/72, 160/110 and 125/80. Shortly before an ECT most patients exhibited signs of an increase in anxiety, and the blood pressure figures were correspondingly higher. The average blood pressure of patients five to ten minutes before the administration of Atropine was 145/96 in the control and 139/89 in the study group. In the latter there was a further increase following the administration of Methedrine. The average blood pressure of patients ten to fifteen minutes after the injection of 10 mg. of Methedrine was 144/96, and 157/101 after 20 mg. of Methedrine.

A considerable variation in the blood pressure changes was observed among individual patients, and to a lesser degree in the same patients on different occasions. This applied to both groups, and could be illustrated by the cases quoted below. The examples selected had the highest absolute figures of blood pressure, and, also, the greatest variations.

(1) A fifty-three year old patient, with a psychotic depressive reaction, had a basic blood pressure of 125/90. Shortly before an ECT it would always go up, and it ranged from 146/96 to 168/100. After 10 mg. of Methedrine there was a further increase with figures from 154/90 to 180/100. Her blood pressure immediately after convulsion varied between 194/100 to 250/120. (2) The highest increases of blood pressure among the controls were observed in a fifty year old patient with an involutional psychotic reaction and a basic blood pressure of 150/100. The increases of her blood pressure shortly prior to an ECT ranged from 162/100 to 180/110 and immediately after convulsions from 205/110 to 260/135. (3) One of the normotensive patients in the same group with a basic blood pressure of 120/84 had her highest pre ECT blood pressure 180/100, and the highest post ECT blood pressure (on the same occasion) 252/120.

The average post EST blood pressure figures in the two groups were quite comparable: 185/107 in the control group, 179/106 in patients receiving 10 mg. of Methedrine, and 189/107 in those receiving 20 mg. It appeared that in both groups those patients who had a higher blood pressure shortly before a treatment would have a correspondingly higher blood pressure immediately after, regardless of whether the pre-ECT increase was due to administration of Methedrine, due to anxiety, or due to some other factors. The overall figures in this study would indicate that the role of Methedrine was less significant in this respect. It was quite negligible when 10 mg. was employed; when 20 mg. was used there was a definite moderate degree increase.

The differences in the pulse rate in the two groups were clinically negligible. The average pulse rate figure before an injection of Methedrine was 97; it would go up to 108 following 10 mg. of Methedrine, and to 112 after 20 mg. There was no appreciable difference between the two groups in the incidence and severity of the transitory arythmias associated with ECT, if anything, these seemed to be less pronounced in patients premedicated with Methedrine.

There were no complications in this study except for the previously mentioned one oc-

casion, when injections of 20 mg. of Methedrine precipitated a state of panic.

Conclusions

The lower average number of electrical shock treatments in the study group is considered as definitely significant, in spite of the fact that it may not have a practical value in routine ECT. It indicates that methamphetamine potentiates the effect of an electrical shock, if not actually changes the quality of it. From observation of the patient (e.g. case histories), it appeared that this kind of treatment may be of a special use in those cases of affective disorders where the prognosis with ECT alone is not too good, and also that it may increase the applicability of ECT in some forms of schizophrenia.

In this respect our findings are similar to those of Fabing.[3,4] However, after personal experience with both Methedrine and Coramine as an adjuvant to ECT, it is the authors' impression that the overall therapeutic results are better when Methedrine is employed. It also has other, more definite advantages, insofar as the intravenous injection of Methedrine produces less anxiety than Coramine, does not have to be timed as accurately as Coramine,[4] and does not cause venous thromboses. Following an electrical shock the patients are more alert and subjectively feel better. The fact that Methedrine does elevate blood pressure may be disadvantageous in treating some patients with a cardio-vascular disease, but otherwise this does not seem to be of any clinical significance.

We conclude that this method is a valuable adjunct to our therapeutic armamentarium. The indication for its application can be made on clinical grounds or on the basis of testing the autonomic nervous system, as in Funkenstein's test. With regard to the latter, it would be very interesting to determine whether or not premedication with methamphetamine or other cerebral stimulants could alter the unfavorable prognosis as predicted by this test.

Summary

A random sample of 25 female patients were treated by electroconvulsive therapy, in which premedication with 10 or 20 mg. of methamphetamine hydrochloride (Methedrine) was used as an adjuvant. The therapeutic results and side-effects were discussed and compared with a similar sample of control patients treate by a standard method.

It was recommended that ECT with methamphetamine hydrochloride as an adjuvant, should be added as another method of our therapeutic equipment.

Authors' Note: Thanks and appreciation are expressed to Burroughs Wellcome & Co. for generous supplies of Methedrine and financial assistance to facilitate this work.

BIBLIGRAPHY

1. Andren, H. E.: Treatment of Depression with Meratran and Electroshock. *Dis. of Nerv. Syst.*, 16:273-276, Sept. 1955.
2. Brussel, J. A., Wilson, D. C., and Shankel, L. W.: The Use of Methedrine in Psychiatric Practice. *Psych. Quar.*, July 1954.
3. Fabing, H. D.: Combined Coramine-Electroshock Therapy in the Treatment of Psychiatric Excitement. *Am. J. of Psychiat.*, 105 pp. 435-438, Dec. 1948.
4. Fabing, H. D.: Seven Years of Clinical Experience with Combined Coramine-Electroshock Therapy, p. 282-7, *Confinia Neurologia*, 14 (5), 1954.
5. Kleinschmidt, H. J.: Preliminary Benzidrinization in Electric and Azazol Convulsive Treatment and Some Observations on Different convulsive Mechanisms. *Harefuah*, 30:10, Jan. 1946.
6. Lennox, M. A., Ruch, T. C., and Guterman, B.: Effect of Benzedrine on Postelectric Shock EEG. *Electroencephalography and Clinical Neurophysiology*, 3:63-64, Feb. 1951.
7. Levine, J., Rinkel, M., and Greenblatt, H.: Psychological and Physiological Effects of Intravenous Pervitin. *Am. J. Psychiat.*, 105:429, 1948.
8. Levy, S.: The Value of Convulsive Therapy in the Aged with Special Reference to Combined Coramine Electroshock Therapy. *Confinia Neurologia*, 12:5-6, p. 381-5, 1952.
9. Diagnostic and Statistical Manual. *American Psychiatric Assn.*

Electroencephalographic Findings in Matricide

(A Case Report)

DON L. WINFIELD, PH.D., and ORHAN OZTURK, M.D.

The objectives of this paper are threefold:

1. To present a brief discussion of the EEG pattern known as "14 and 6 per second positive spikes."

2. To present a case report of a 13 year old boy who shot and killed his mother.

3. To present the comparative results of various activating techniques including metrazol, Pentathol, hyperventilation, sedative induced sleep and photic stimulation on this particular patient.

The EEG pattern designated "14 and 6 per second positive spikes" was described by the Gibbses[1] in 1951. This proved to be one of the more controversial issues of recent years, but the impressive data presented by the Gibbs, Kellaway,[2] Schwade,[3] etc., have convinced more and more electroencephalographers, particularly those experienced in the interpretation of sleep tracings, that this is an important EEG abnormality.

Positive spikes are associated with a variety of symptoms with the etiological agent usually unknown, although head trauma and encephalitis are the two most frequently presumed etiological agents. The pattern in itself is not a seizure discharge but a sign of dysfunction which may have epileptiform manifestations. The symptomatology of patients with these patterns combined with pathological findings, experimental data and the field of the discharges suggest involvement of the sub-cortical areas, particularly the thalamus and hypothalamus.

This abnormality is commonly seen in the severe behavior disorders and consequently the possibility of positive spikes became immediately apparent when a 13 year old boy, who shot and killed his mother over a trivial incident on January 29, 1957, was referred for EEG studies. The presence of organicity was suggested by a history of behavior difficulties with hyperactivity as a major complaint. There was also history of speech difficulty and a period of persistent unexplained fever which required hospitalization for about 10 days at the age of seven in March 1951. At that time he reportedly had an abnormal EEG with the interpretation of "Suggestive generalized cortical dysfunction compatible with some form of generalized epilepsy." He was seen in a Neurosurgical Clinic in June 1951 and because of the abnormal EEG was placed on Dilantin 0.03 gr. t.i.d. In July of 1951 no improvement was noted and phenobarbital 0.32 gr. t.i.d. was added. The patient became more hyperactive and the phenobarbital was stopped. In August he was placed on Thiantoin 0.12 gr. daily and the Dilantin was discontinued. The Thiantoin increased the incidence of nightmares which the child had been having and this medication was discontinued. An EEG in February 1954 was reported as normal. Several EEG's done since have been reported as normal. These tests were done in another city where sleep tracings were the exception rather than the rule and it was felt that the child did not have adequate EEG studies.

Before presenting the results of the EEG studies on this patient, additional history and clinical data obtained from the records of his previous hospitalizations are as follows:

The patient had a full term uncomplicated birth, weighed 7 pounds and 5 ounces. He was breast fed; walked and talked at one year, but stopped talking until he was 3 years old. The father who was in the service did not see him until he was one year old and then the patient would scream when the father entered the room. When the child was 3 the father would "knuckle" him on the head. At 5 years of age he was referred to a speech clinic for speech therapy which continued through the fourth grade. He had few friends, primarily because his mother would not let him play with other children for she felt that the other children in the neighborhood were not good enough

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for him. He was hyperactive and had occasional violent fits of temper which led to his referral for psychiatric treatment in February 1954. His current teacher indicated that the patient was an "average" student but a "nervous" child. He was hyperactive and talked a great deal during school but was not considered a behavior problem. By contrast, an older sister has always been an excellent student and was favored by both parents. The patient described the sister as "mean, hateful, or something like that—if you had a sister older than you, you may know what I'm talking about."

Perhaps the only other significant medical history was the recurring episodes of otitis media beginning at the age of three and these have persisted. Temperature elevations have been common with these illnesses.

The father is described as a very rigid person who displayed no emotion over the fact that the patient had killed his mother. The mother was orphaned at an early age, was talkative, and domineering. The patient stated, "Mom can whip hardest with a broom handle, fly swatter, or her shoe."

A maternal uncle died in a mental institution and the mother had psychiatric treatment as well as case work services from several agencies. Two maternal uncles have had difficulties with the courts and have served terms in the penitentiary. A maternal aunt has had two illegitimate children.

The day of the murder was described as a usual school day except he may have been "sort of tired and had the blues—I might and I may have not, but felt angry—I had no friends—everybody seemed mad and I felt lost." He related being "mad" before he had gotten home—"one of those rough days, nothing happened right."

A summary of his sworn statement given the day of the murder is as follows:

On the afternoon of January 29, 1957, the patient was playing with a book of matches on the table. His mother made him stop. She also refused to let him play with his switchblade knife and said something "sorter fussy." The patient went to his room, loaded his father's 22 rifle with bullets he had taken two days previously and returned to the living room where his mother was sitting at a table reading with her back toward him. He stood at the door and shot her in the head. She fell to the floor. He pulled the trigger again but it did not fire. Then he shot her again while she was lying on the floor. He felt her heart to see if it were beating and it was. He packed his suitcase and checked his mother again. She was still alive and asking for help. He left the house, visited a friend until apprehended by the police that evening.

On June 30, 1957, the patient was referred for observation and study at a state hospital. He was an excellent patient and showed no overt evidence of aggression or hostility at any time. He has never shown any guilt or remorse over the killing of his mother. In fact, there has not been any overt emotional reaction. There have been no psychotic manifestations, feelings of guilt or anxiety. The patient occasionally complained of abdominal complaints unassociated with hunger. The psychiatric staff unanimously agreed that the boy is abnormal but disagreed as to the psychiatric diagnosis of his being psychotic. The child was returned to the juvenile court April 4, 1957, with a diagnosis of "Not insane" in the legal sense. On April 5, 1957, a hearing was held concerning the murder, and the judge ordered the patient committed to Gailor Psychiatric Hospital, Memphis, Tenn., for further observation and treatment. The patient was admitted April 8, 1957, and our series of tests began April 10, 1957. The EEG findings are as follows:

1. 4/10/57 normal awake and during hyperventilation. No sleep with 300 (200 and 100) mg. Noludar (Fig. 1).

2. 4/11/57 positive spikes in right-temporal-occipital area in sleep. 600 (300 and 300) mg. Noludar (Fig. 2).

3. 4/17/57 Goldman's technique of IV pentathol—300 mg. and no sleep. ? of Pentathol effects. Photic driving but no seizure activity (range of 4-10 cps) (Fig. 3 a & b).

4. 4/23/57 425 mg. IV metrazol (Merlis technique) no activation. No sleep with 7½ gr. IV Na. Amytal.

5. 4/25/57 Positive spikes in the right-temporal-occipital area in sleep. Up till 1:00 a.m. and 300 mg. Noludar.

6. 5/2/57 500 mg. metrazol and photic stimulation followed by IV Amytal (300 mg.). Positive spikes in right-temporal-occipital area during sleep (Fig. 4 a & b).

This seems to be rather convincing evidence that the sleep tracings produced the most significant EEG findings. One might speculate that the recurrent bouts of fever were associated with a cerebral infection

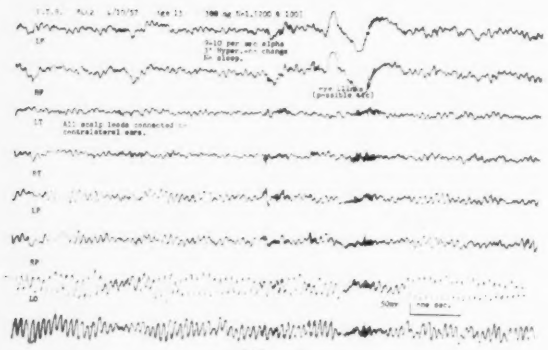

Fig. 1.

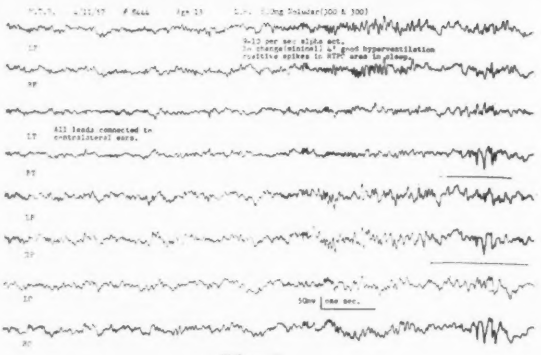

Fig. 2.

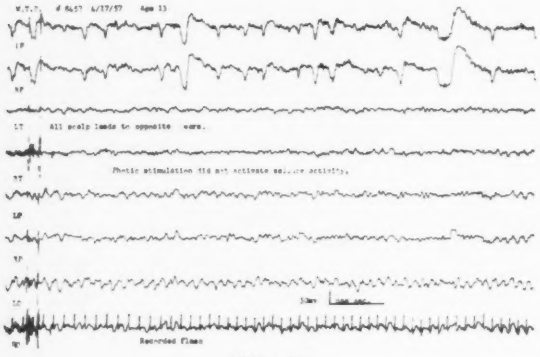

Fig. 3a.

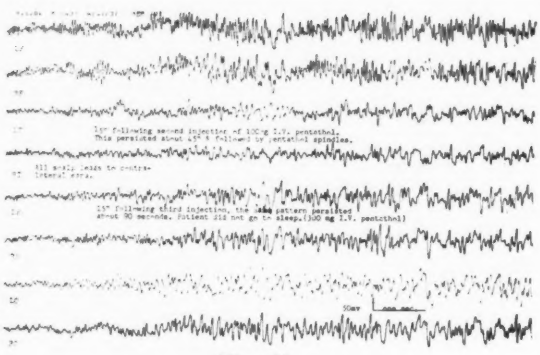

Fig. 3b.

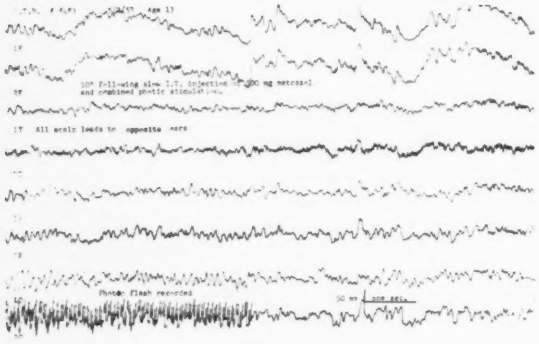

Fig. 4a.

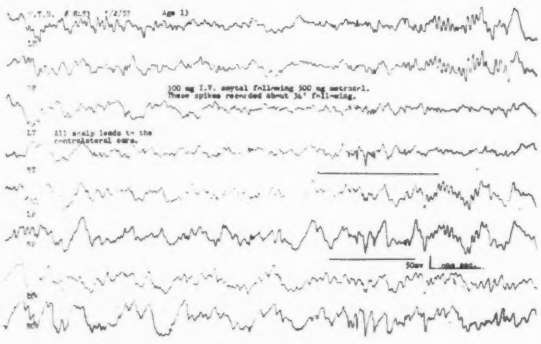

Fig. 4b.

with the resulting behavioral difficulties and positive spikes. The psychological examination also suggested an organic factor in the patient's illness.

The diagnosis has not been fully established for this patient. He refuses to give the "real" reason for the killing. His therapist states that he has an excellent sense of humor, is pleasant, obedient, cooperative, reveals no thought disturbances and has good affect; except in reference to the killing. In any event the sleep tracings have produced additional data that suggest a neurophysiological disorder which might conceivably be the basis for the patient's deviant behavior.

REFERENCES

1. Gibbs, F. A., and Gibbs, E. L.: EEG Evidence of Thalamic and Hypothalamic Epilepsy. *Neurology* (Vol. I, No. 2), March-April, 1951.
2. Kellaway, P., Moore, F. J., and Kagawa, N. J.: The "14 and 6 per Second Positive Spike" Pattern of Gibbs and Gibbs. Presented at the meeting of *American EEG Society,* Atlantic City, New Jersey, 1956.
3. Schwade, E. D., and Geiger, S. G.: Abnormal EEG Findings in Severe Behavior Disorders. *Dis. Nerv. System,* 16:2-12, 1955.

Effects of Music and Recreation Upon Patients Receiving Electro-Convulsive Therapy

GERALD O'MORROW

The therapeutic value of music and recreation has been noted since early times. Music in conjunction with pre and post electroshock treatment has been reported by Altschuler, Leedy and Leedy, Price, Kotter and others. After having read much of the literature concerning recreation as a therapy, this author has been unable to find any reports in its use as an adjunctive therapy to treatment. With this in mind the following research project was investigated.

Since no account of an experimental study in this area has been found this study is on an exploratory basis with three factors in view.

1. To determine whether music and recreation together in the waiting room would reduce the fear and anxiety of the patients before electro-convulsive therapy.
2. To determine the specific therapeutic value of music alone, recreation alone, and music and recreation together in the waiting room.
3. What effects (physiologically) on a verbal level does the patient express when no music and music is offered in the recovery room.

Electroshock was administered in a room primarily arranged for the treatment; the waiting and recovery rooms adjoined the treatment room through a hall. Patients went to the waiting room approximately five to ten minutes before treatment. No pre-medication was given on the ward before the patients went to the shock suite. Treatment itself was administered with a standard apparatus using both glissando and instantaneous technique modified by administration of oxygen and a muscle relaxant (12 mm Anectine). No other sedation was given during or after treatment.

The research plan included a two-week general observation period, a four-week period concerned with factor number one, an evaluation of the period, and a three-week final study concerned with factors number two and three.

From Napa State Hospital, Imola, California.

Prior to the study a meeting was held with the ward doctor, nurses, and psychiatric technicians on the shock team. The purpose and method of the study was explained. The two-week general observation period was used to observe the patient's behavior and help the shock team to become familiar with the method of rating and observation.

The selection of music, which was used through the study was of the type usually referred to as "mood-music" (Montavani and His Orchestra, The Melachrino Orchestra, Music For Relaxing, Music for Daydreaming, etc.). Selection of this style of music is based upon the suggestion of Altshuler[1] who states that "the familiar tune does not only revive an angram—a basic reality—but helps to relieve emotional tension. Through a familiar song or melody . . . pleasant or unpleasant experiences can be abstracted."

The use of mood-music seemed to have a better effect upon the patients than classical music which is contrary to what some writers have found in their experiments with music in pre and post electro-convulsive therapy. Attempts were made to use classical music in both rooms during the general observation period, but the patients appeared to be more confused, restless, hostile, and showed more convulsive excitement as compared to when mood-music was played.

Since the shock team was able to hear the music in the treatment room they stated that the music (mood-music) helped to relax them and made the treatment process less monotonous. Unkefer[7] has observed that music has proved beneficial to working personnel doing repetitious work.

Space of the waiting room limited the equipment to passive type games and these games selected on an exploratory basis included: Chinese checkers, cards, checkers, scrabble, Po-Ke-No, and a ball attached to a wooden cup by a string. Two tables were provided for the games.

The design was as follows for the waiting room:

	Monday	*Wednes.*	*Friday*
1st week	Music	Music and Recreation	Recreation
2nd week	Music and Recreation	Recreation	Music
3rd week	Recreation	Music	Music and Recreation

The design for research in the recovery room was a staggered schedule of music being offered every other day and followed by a silent day.

A rating scale consisting of the following items was used in the waiting room on the final study: 1) Very relaxed, 2) Relaxed, 3) Restless, mildly apprehensive, 4) Tense, 5) Resistive. The patients were graded as a whole rather than individually and all grading was done by the shock team after treatment was terminated for the day. Each member of the shock team was requested to check one of the five items on the rating scale which the patients as a whole exhibited in their behavior.

After treatment the patient was removed to the recovery room on the same bed in which he received treatment and upon returning to consciousness was removed to a sitting position on the floor. Three questions were asked of the patients approximately twenty minutes after treatment (treatment beginning between 8:30 and 9:00 a.m.) and repeated at 3:00 p.m. of the same day. The questions asked were the following:

1. How do you feel?
2. Do you hear any music?
3. Do you know who I (therapist) am?

The average number of patients receiving treatment per day was 20.

Factor number one was determined through observation by the various members of the shock team and the therapist. Results based on this type of observation are not always conclusive. The study indicated that music and recreation decreased the fear and resistance to electroconvulsive therapy and helped to eliminate tension. These results are very similar to the findings of Leedy and Leedy,[4] except that they used music alone. The value of recreation is shown in the fact that 64% of the patients participated in recreation games.

Results based on the rating scale used to determine factor number two, showed that 30% of the patients appeared to be relaxed when music only was offered as compared to 71% with recreation and 65% with music and recreation together. Furthermore, 20% of the patients appeared to be restless and mildly apprehensive when recreation was offered compared to 5% with music, and 17% with music and recreation together. Tension was noticed 13% of the time when music alone and music and recreation together was offered compared to 2% with recreation alone.

It is difficult to say that music is a better adjunctive therapy to this kind of treatment than recreation. Although music scored high in helping the patients to relax, it also had the highest recorded percentage of tension, while this one factor existed minimally when recreation was used alone. It is possible that recreation could be the same value as music is today in pre electroconvulsive treatment, if the right type of game could be developed.

To satisfactorily treat diseases, all specialties of medicine must treat the patient as an individual, which means recognizing that each patient is a whole being with feelings and emotions. It is then unlikely that music and recreation in pre-shock treatment could produce alleviation of any somatic pain which many of the patients expressed, but it surely relieves the apprehension of the patients approaching treatment.

Table I and II show the results of participation in recreation games in the waiting room.

TABLE I

Recreation Alone

Chinese Checkers	10%
Cards	14%
Wooden cup	4%

TABLE II

Music and Recreation Together

Chinese Checkers	18%
Cards	11%
Wooden cup	3%

Table II points out that more patients participated in recreation when music was offered. It is possible that music helped relieve some of the tension and so made it

easier for the patients to accept and participate in recreation, while recreation alone was to some extent just a silent period.

Response to questions asked in the recovery room when music was offered showed that the feelings of the patients (dizziness, headaches, head hurting, sleepiness, nausea, and feeling of well being) and recognition of the therapist improved 10% compared to 8% improvement with no music. The interviewer asked additional questions to clarify the responses when necessary.

A number of other factors should be pointed out regarding the recovery room.

1. There was a 4% decrease in patient's feeling of well being as the day progressed with no music compared to 8% increase when music was offered.
2. Dizziness and sleepiness increased 8% respectively as the day progressed, regardless of whether there was music or no music.
3. The ability to recall music upon awakening was 52% compared to 20% who were unable to recall music.
4. Other general factors noted in the recovery room after return to consciousness were less convulsive excitement, confusion, and enthusiasm of the patients to return to the ward.

Patients who were unable to respond to any questions were classified as "very confused." If they were able to answer one or two questions out of three they were checked "confused." Nearly all the patients who were classified "very confused" were those who were on their third or fourth treatment.

The number of patients interviewed for the recovery room study, whether there was music or no music, was 125. At times the number of patients varied because some were discontinued and others added. The same patients were used for both music and non-music days.

From published reports[1,2,5,6] verbalization seems to correspond with waiting, and because of these findings the questioning of the patients began approximately twenty minutes after treatment, although some patients were not asked questions until thirty or forty minutes after treatment. The efforts of the patients to re-establish their orientation became very clear when asked, "Do you know who I am?" As reported above, 52% were able to recall the therapist; but only half of these were able to recall where they had last seen the therapist, and these were patients who were asked thirty to forty minutes after treatment. These answers usually followed in this manner, "Yes, I have seen you but..."

It is difficult to give any real reason why dizziness and sleepiness increased during the day while improvement of other feelings and symptoms could be explained by the removal of emotional distress, interest in other therapies (recreation and occupational therapy), and attention to personal habits.

In summary, this report is an investigation into the effects of music and recreation in pre electroconvulsive therapy and the physiological effects on patients with music in post electroconvulsive therapy. The design in pre electroconvulsive therapy was a staggered schedule of music alone, recreation alone, and music and recreation together, with three treatments weekly for three weeks. A rating scale was used, and it was found that although music alone has a slightly greater effect than recreation alone in helping the patient to relax, it cannot be said that recreation alone was not beneficial. It was demonstrated that a large percentage of the patients were shown to be tense when music was offered, while with recreation it scarcely existed. The effects on the physiology of the patients showed that on the day music was offered the patients felt better as the day progressed as compared to a slight decrease in feelings when no music was offered.

REFERENCES

1. Altshuler, I. A.: Four Years' Experience with Music as a Therapeutic Agent at Eloise Hospital. *Am. J. Psychiat.*, 100-792, May, 1944.
2. Kalinowsky, L., and Hoch, P. H.: Shock Treatment, Psychosurgery and Other Somatic Treatment in Psychiatry. N. Y.: *Grune and Stratton*, 2nd ed., 1952.
3. Shatin, L., Gilmore, T., Kotter, W.: A Study of the Relationship Between Music and Post-Electroshock Awakening. *Dis. Nerv. Syst.*, 15 (8): 250-253, 1954.
4. Leedy, J. J., and Leedy, D. J.: Use of Music with Electro-convulsive Therapy. *Dis. Nerv. Sys.*, 12: 281, Sept., 1951.
5. Lowenbach, H., and Stainbrook, E. J.: Observation on Mental Patients. *Am. J. Psychiat.*, 98: 828, 1942.
6. Stone, C. P.: Losses and Gains in Cognitive Functions as Related to Electro-convulsive Shock. *Abn. & Soc. Psych.*, 42:206, 1947.
7. Unkefer, R. F.: The Effects of Music in Insulin-Coma Therapy. Music Therapy, *NAMT*, Chicago, 184, 1951.

Psychoenergetics

THEODORE R. ROBIE, M.D.

During the past two years a revolution has taken place in the treatment of melancholic psychiatric disorders. Although Freud is recognized as the father of modern psychiatry in the psychological sphere, it is less well known that he also believed that ultimately some of the major psychological disorders might become understandable in physiological or chemical terms. It is not surprising that when chemicals that could energize the depressed psyche were discovered, a word first used by Freud, "Psychoenergetics," should emerge as the most succinct term to describe this area of research.

We have witnessed the introduction of a number of chemical substances capable of reversing suicidal depression in a large proportion of cases. Thus the need for electroshock therapy has been supplanted in over 50% of the melancholy patients treated. This proportion should increase as new chemicals are discovered, making possible even faster remission of depression. Iproniazid (Marsilid®-Roche), the first of these astonishing new drugs, has proved capable of producing remission in a major percentage of depressions treated with adequate dosage. It has led all other chemotherapeutic forms of treatment in this field. However, it has produced some undesirable side effects. Various other amine oxidase inhibitors are being introduced and the possibility looms that one of these will accomplish the objective of overcoming melancholia without side effects.

In previous papers,[2,3,4] the relative advantages of chemotherapy over electrotherapy for overcoming melancholia were delineated. During the past year further experiences have corroborated this earlier work, which had convinced me that a great many melancholia victims could be spared the hazards of electroconvulsive therapy by judicious use of amine oxidase inhibitors (A.O.I.), combined with cathartic psychotherapy.

The following case illustrates this point:

A 40-year-old man who had been depressed for several years (the illness going unrecognized by his family), made several suicidal attempts. However, in three successive attempts to discharge the gun held against his temple, the revolver (unused for years) failed to discharge. Thus thwarted in his suicide aim, he returned to his home and admitted the attempt to his wife. I was consulted and I started him on iproniazid immediately. Within a few weeks his spirits were raised to a level unknown to his family for several years. In less than a month he returned to the job which he had blamed for his melancholia. With his present good spirits (chemically induced) he should be able to reorganize his life by finding a more satisfying job, while temporarily remaining at his seven days per week "depression"-aggravating job—the straw that broke the camel's back! Only a short time ago electroshock would have been imperative for this man, but with today's knowledge his melancholia has been overcome by chemical means and he was restored to vocational productivity in less time than would be possible with electroshock therapy.

Any medication is truly remarkable that can alleviate melancholia and save the patient and his relatives from the emotional turmoil induced by the contemplation of electroshock therapy! Despite the fact that electroshock therapy will induce remission of melancholia and thus prevent suicide in 80% to 90% of cases, the fear of electricity often prevents the patient's agreeing to treatment. Quite a few melancholics will refuse to undergo treatment, even though the psychiatrist endeavors to convince them that electrocerebrotherapy can be made painless and harmless by anesthesia combined with chemoparesis. Such patients, committed to a hospital where electric therapy may be given, even against their will, often do not get it because their spouses cannot believe they would ever commit suicide despite long-time threats of self-destruction. There is no way to return life when suicide is successful! Yet, many potentially suicidal persons, who refuse electric treatment, would cooperate in a course of chemotherapy via simple tablets taken while they stay at their occupation. As eudaemonia gradually develops the suicide urge is dissipated.

The amine oxidase inhibitors are in this "magical" category. However, in the words of Dr. Dale Friend of Boston,[5] "We owe it to all our patients to carry out every possible known test that will protect the patient, whenever giving any drug that is known to

be dangerous." Just as the dose of Dicumarol must be reduced or stopped in accordance with the prothrombin time, so must dosage of A.O.I. be reduced or stopped if we have any indication of liver pathology. I believe we now possess an instrument of inestimable value in reducing the liver complications that have understandably dampened the enthusiasm of proponents of this chemotherapy.

"Research" implies that "a search is in *process,*" and not necessarily *"completed."* Therefore a report of a study reasonably will suggest new ways to improve efficiency in treatment. The laboratory method to be described is one of these. One fund of available information suggests that iproniazid may in rare instances initiate the chain of physiological events resulting in fulminating hepatitis with an estimated mortality of 1 per 16,000 to 1 per 25,000 cases receiving iproniazid. This form of hepatitis has been likened to viral hepatitis. Even though pathologists cannot determine via the microscope whether "virus" hepatitis is the true cause of death in such cases, it must be recognized that iproniazid allergy or other noxious influence may be the initiating factor.

Felix Wroblewski, of Memorial Hospital, New York, has shown that frequent determinations of the serum glutamic-oxaloacetic transaminase (SGO-T) may serve as a warning that minimal hepatic necrosis is developing. If discovered early enough, it may enable us to discontinue the offending medicine, or to prevent its hepatotoxic effects, in time to avoid generalized liver necrosis. Let us suppose that the SGO-T is 24 units on January 1st, 20 units on January 7th, 32 units on January 14th, and then jumps to 69 units on January 21st. Since the normal level is 40 units or less, this increase should be a warning to discontinue iproniazid immediately. Further SGO-T tests would tell whether mild hepatitis had been reversed; further treatment may be guided by this test. Small doses of iproniazid may be tolerated later with low doses of cortisone or ACTH as supportive therapy, while frequent transaminase determination continues to guide the therapeutic program.

We may then discover that the patient can maintain adequate eudaemonia without further iproniazid therapy, or that Ritalin or some other euphoriant may be adequate to maintain the improved status originally induced by iproniazid therapy. At this point the slowly developing constructive effects of Deaner may prove adequate for maintenance of eudaemonia. However, the psychiatrist must be alert to detect sudden regression into deep melancholia from abrupt withdrawal of the chemical prop.

A 28-year old woman whose vocation demanded constant alert mentation, was brought out of a pronounced state of melancholia within a few weeks, following initiation of iproniazid therapy in the usual dosage of 150 mgs. daily. The dose was reduced to 100 mgs. after a few days, but had to be kept at this level for several months to prevent return of depression and loss of the 4 pounds gained on the higher dose. However, by the fourth month with the help of supportive psychotherapy, the dose could be further reduced. During the 8th month of treatment she still needed 50 mgs. daily, any reduction brought on mild recurrence of melancholic behavior. This patient proved to be the first in our experience whose transminase level was high in spite of complete lack of jaundice. Thus, because of an 83 unit SGO-T report iproniazid was abruptly discontinued. In 3 days there was definite emotional disturbance and after 5 days sobbing at frequent intervals became so uncontrollable that she had to cease work. She was placed on Ritalin which partially lifted the heavy melancholia, but not sufficiently to prevent recurrent outbursts of uncontrolled sobbing. Since no suggestion of jaundice had appeared, smaller doses of a new amine oxidase inhibitor (RO 5-0831/1) were tried with an almost immediate and miraculous return of her former iproniazid-maintained sense of well being, and joyful, energetic return to her gainful occupation. It was later discovered that the pathological SGO-T report of 83, was an artefact, because subsequent determinations have all been within the normal range. The patient meanwhile continued in excellent eudaemonia having regained quickly her self-confidence, attained during the 9 months before iproniazid was stopped.

Not all cases show such a sudden relapse into depression when iproniazid is withdrawn, but this case showed dramatically how serious the problem can be for the psychiatrist who finds it necessary to interrupt the amine oxidase inhibitor. The lesson to be learned is that for the average case with no side effects, when weaning is planned, the dosage should be lowered gradually from 25 mgs. to 5 mgs. every second or third day until all depressive reaction is definitely eradicated. This may require 6 weeks or longer.

An important technical point about the transaminase test is the manner in which it is presented to the patient. Most of our patients are over-anxious, some more than others, but almost any of them would become more apprehensive if the complete clinical facts were presented. I have found that an explanation such as this is helpful and usually allays apprehension: "We find that we can judge the dosage you will need by this test done frequently during the early period of treatment. It will not be necessary quite as frequently when the dosage is lower."

For those who are more demanding, an outline of the mechanics involved in the prothrombin test for those persons taking Dicumarol can help the patient realize how necessary this transaminase test is. The doctor can also explain why blood sugar tests are done in diabetics which may help them better to understand the transaminase test. The unfortunate and sensational newspaper stories have made it more difficult to secure a patient's cooperation in taking a drug that may literally save his life. However, when convinced that these tests make its administration a safer procedure, the patient will cooperate fully in most instances.

Until the time comes when we have discovered a reliable method of preventing serious complications, the path of the clinician using this drug will not be strewn with roses. However, we cannot abandon a therapy that has so dramatically proved its value, any more than we could have abandoned electroshock therapy in the early days when many complicating fractures occurred. Eventually we learned how to prevent the fractures by Anectine muscular relaxation. In the early days of anesthesia, surgery and all other major medical advances, unexpected complications resulted in occasional deaths, and such hazards are far from eradicated even today. Let us not forget that mortality from tonsillectomy, long considered a time-tested relatively safe procedure, is actually between 1 in 2,000 and 1 in 10,000, and thus iproniazid is at least 8 times safer.

A starting dose of 150 mg. of iproniazid is necessary whether the patient is treated in or out of the hospital. If an inadequate dose is given the response may be delayed to the point of greatly increasing the danger of suicide, thereby defeating our very purpose.

In an editorial in The Journal of the American Medical Association (150:696-697 Oct. 8, 1952), calling attention to suicide as a leading cause of death, deep moods of depression, active conflict, anxiety, and withdrawn resignation are emphasized as especially significant in persons with suicidal inclinations. If we make the conservative assumption that only a third of the 20,000 estimated suicidal patients during 1958 are suffering from some degree of depression we can speculate on what might happen if these 6,000 patients were placed on therapy with iproniazid. According to the present estimated morbidity and mortality figures associated with iproniazid therapy, a maximum of two of these 6,000 patients might be expected to develop jaundice. These two patients then have a 75% chance of surviving hepatitis without serious consequences. Let us assume, for the moment, a 10% efficacy of iproniazid treatment in depressed patients (and some have claimed better than 80% effectiveness of the drug.) In that case, of the 6,000 patients, roughly 600 would have a chance to survive 1958 without committing suicide, if they were treated with iproniazid. Actually, we may expect that many more than the 600 might remain alive if iproniazid were administered to all who were depressed.

A comparison of another mode of treatment of depression, namely, electroshock therapy (EST) will disclose that the "calculated risk" of mortality is markedly less with iproniazid. Mortality is 1 per 1,000 patients treated with EST (Impastato), while from the most reliable statistics available, Jolly estimated that the mortality with iproniazid is 1 in 16,000 to 25,000 patients under treatment. Thus, iproniazid is at least 16 times safer than the only other recognized treatment for preventing suicide in melancholia. Quite apart from mortality is the fact that, during EST the necessary loss of time from employment (5 or 6 weeks) may militate against the patient's retaining his job, a factor crucial to eliminating the melancholia and to preserving his life. Furthermore, one can hardly ignore the economic factor involved, both in the loss of time from

work and the three times higher cost of EST, as compared with that of iproniazid therapy.

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130 Bellevue Ave.
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BIBLIOGRAPHY

1. Kline, N.: Symposium on Amine Oxidase Inhibitors. New York, Nov. 21, 1958.
2. Robie, T. R.: Marsilid and Electroconvulsive Shock Therapy. *J. Clin. & Exper. Psychopath.*, June 1958.
3. A New Pharmacotherapeutic Approach in the Treatment of Melancholia. *Assoc. for Research in Nervous & Mental Dis.*, 1957.
4. Marsilid versus Electroshock in the Treatment of Melancholia. *N. Y. Neurol. Soc.*, Apr. 8, 1958.
5. Statement made as Chairman of the Symposium on Amine Oxidase Inhibitors at the Hotel Barbizon-Plaza, Nov. 20-22, 1958, under the auspices of the *New York Academy of Science*.
6. Robie, T. R.: Toxicity of Iproniazid. *J.A.M.A.*, p. 1802, Nov. 29, 1958.
7. Wroblewski, F.: Clinical Signicance of Serum Enzyme Alterations Associated with Myocardial Infarction. *Am. Heart J.*, Vol. 54, p. 219, 1957.

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